THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—24TH YEAR. SYDNEY, SATURDAY, AUGUST 28, 1937. No. 9.

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EPILEPSY AS A SYMPTOM OF ORGANIC LESIONS OF THE BRAIN.[1]

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EPILEPSY, as a symptom, may because of its dramatic features assume overwhelming importance from the patient's, or his relatives', point of view; and it may be equally important to the physician as the only symptom of which the patient complains. Sir William Gowers[1] defined epilepsy as:

> The recurrence of sudden brief disturbances of some function of the brain, varying in degree, extent and character, but generally attended with an arrest of consciousness sufficient, at least, to interrupt the control of muscles necessary for the maintenance of the erect posture.

It will be noticed that no mention of muscular convulsion is made in this definition. Hughlings Jackson considered

> epilepsies on the hypothesis that the paroxysm is dependent on a sudden temporary excessive, disorderly discharge of some highly unstable region of the cerebral cortex.

Let us consider the case of a patient who presents this symptom. The first problem is this: Is the patient suffering from idiopathic epilepsy or is there a cause which can be discovered? In this connexion it is well to remember what has been so admirably stated by Monrad-Krohn:[2]

> In the whole medical nomenclature there is no word so false as genuine, so misleading as idiopathic and so unessential as essential. They are just words to cloak our ignorance.

[1] Read at a meeting of the Victorian Branch of the British Medical Association on June 2, 1937.

In idiopathic epilepsy the cause is, as yet, undiscovered; in the symptomatic form one of the many known causative factors is present. In considering many of the problems of epilepsy, it is helpful to consider that there is an underlying "epileptic tendency", in the presence of which many factors may precipitate an epileptic attack. This explains the variable presence or absence of the symptom in cases in which the pathological lesions appear to be identical; for example, its presence in some cases of cerebral tumour or uræmia, and its absence in others. There can be little doubt that there is a precipitating factor in all cases of epilepsy, but in the idiopathic disease it is as yet unknown. Subtle metabolic and endocrine factors are probably responsible for some of the "idiopathic" convulsions. The later the attacks commence in life, the more likely is there to be an organic cause. It is important to inquire directly for a history of convulsions in infancy, the presence of attacks of *petit mal*, and the existence of myoclonic jerking of muscles.

Gowers,[1] in an analysis of 2,383 cases of chronic epilepsy, found that 13·5% commenced during the first three years of life. The numbers of cases then fell until the fifth year group (2·4%), which was the smallest for the early period of life. Then a considerable rise occurs at seven (4%), a fall at eight, and then the numbers slowly increase until the maximum is reached at fourteen (7·7%). Then a rapid fall occurs at the twenty-first year (2·7%), after which only a small number began in each year. The convulsions of idiopathic epilepsy are usually generalized, although auræ and localized convulsions do occur when there is no other reason to consider an organic origin.

The history of one patient, a male of twenty-two years (Case I), may be briefly outlined.

> Ever since the patient can remember, he has been having fits. He sees dots of all colours in the right field of vision, and then experiences a drowsy feeling which gradually merges into unconsciousness which lasts for about ten minutes. After the attacks he feels exhausted, and may suffer from headaches for the rest of the day. Before the age of fourteen, his right arm would flex behind his back during the early part of the attack. X ray films of the skull revealed no abnormality. The cerebro-spinal fluid was normal, and encephalography demonstrated normal cerebral ventricles and subarachnoid space.

There can be no doubt that an unstable area exists in the left cerebral hemisphere; but many such cases have been examined pathologically without definite reason having been found to exclude them from the idiopathic group.

It is possible that many such fits are the result of local cerebral lesions sustained in early life. After this brief reference to idiopathic epilepsy, this paper will deal with epilepsy of organic origin in which pathological lesions are present. The essential features of a number of illustrative cases will be briefly described, except in two instances, in which fuller details will be given. The pathological nature of several lesions will be indicated only very briefly, for further study is necessary to elucidate some of them.

Localizing Value of Seizures.

As the history from the patient or witness of attacks unfolds, the question as to whether the epilepsy is a localizing symptom may be solved. Direct observation of an attack may be necessary.

Basing his opinion upon the evolutional doctrines of Laycock, Hughlings Jackson asserted that the substrata of mentation are sensori-motor processes, for:

> of what substance can the organ of mind be composed, unless of processes representing movements and impressions; and how can the convolutions differ from the inferior centres, except as parts representing more intricate co-ordinations of impressions and movements in time and place than they do?

The convolutions of the cerebral cortex contain processes representing movements and impressions and a "brutal discharge" of these cells, he asserted, produces the manifestations of epilepsy. By pure reasoning, he deduced that motor convulsions arose from the convolutions near the *corpus striatum*, and that these convolutions must contain the cells effecting normal movement. If a convulsion commenced with movement of a certain part, he stated that there would be a discharging lesion of the part of the convolution of the opposite hemisphere, the normal function of which was to cause movement of the part affected. The theory was substantiated in 1872 by the finding of a "coarse" lesion (a tuberculoma) in the posterior part of the third frontal convolution of the brain of a patient who had suffered from attacks of epilepsy commencing in the thumb. In 1873 the experimental stimulation of animals' brains by Ferrier produced dramatic confirmation of the philosopher's writings. In describing the slow spread of motor convulsions, of a type which has since come to be named Jacksonian, he knew that he was describing the organization of the precentral convolution:

> The march of the attack, the order in which the different parts of the body become involved, reveals the arrangement of the corresponding foci in the precentral convolution.

Such convolutions, he poined out, begin in the parts having the most varied uses and, therefore, the most extensive cortical localization.

> Fits beginning in the hand are common, fits beginning in the cheek and tongue are less frequent, fits beginning in the foot are rare. The law is to be exemplified in details. For again, taking numbers of cases, the fits which begin in the hand begin usually in the index finger and thumb; fits which begin in the foot begin usually in the great toe.

The unstable part "stores up" energy, and when it reaches a certain degree of instability, discharges are easily provoked. He discussed the difference between the sudden brutal discharge of a group of cells and the selected action of many cortical cells, not necessarily contiguous, producing voluntary movement. The degree of spread of the epileptic process was assumed to be the determining factor in loss of consciousness. He also drew many deductions concerning the bilateral cortical representation of muscles which have withstood the test

of subsequent experimental work. Thus muscles which habitually work in unison, for example, trunk, respiratory and pharyngeal muscles, are represented equally on both sides of the hemisphere; the muscles of the face, particularly the *orbicularis oris*, are still strongly represented on the same as well as on the opposite side. Proximal muscles of the limbs have a weaker ipsilateral representation, and the highly specialized movements of the fingers are represented almost entirely upon the opposite side of the cortex. He considered that the direct pyramidal tract was the anatomical pathway for the ipsilateral efferent impulses. Many of these points are exemplified in the following histories and illustrated by cinema films of the convulsions.

Frontal Lobes: Precentral Convolution.

CASE II.—The patient suffered from fits which commenced with tonic deviation of the mouth to the right side, followed by fine clonic convulsion of the muscles of the right side of the face, which were obvious, as they became coarser, on the left side of the mouth. The movements were never as powerful on the left side of the face as on the right. After the movements had subsided, it was noticed that the right eye did not blink, indicating a degree of post-epileptic paralysis. On exploration, a meningioma was found to be pressing upon the inferior end of the left ascending frontal convolution.

CASE III.—Following a period of emotional instability, the patient, six months before admission to hospital, noticed a nasty feeling in the right hand as though the muscles were tight and unable to relax. Following this, the right arm and hand seemed weak and she had difficulty in writing. A week before admission to the Royal Melbourne Hospital, the patient suddenly lost consciousness for several hours. After recovery, the right hand twitched powerfully at intervals for two days, and it felt dead, numbed and powerless. She was unable to speak on the first day, and on the second had a severe motor aphasia, with difficulty in finding the right words and in the construction of sentences.

On examination, she had slight right facial weakness, gross weakness of the right arm and complete paralysis of forearm and hand muscles, with a slight increase in tone of the flexor muscles. Discriminative sensibility was impaired in the right hand. The twitching of the abductors and flexors of the shoulder and supinators and flexors of the forearm, shown in the film, occurred on the day of operation. The small astrocytoma found, after death, just under the surface in the middle of the ascending frontal convolution, was not identifiable at operation.

CASE IV.—The patient, a woman of fifty years, suffered for fifteen years from convulsions, commencing in the foot and spreading up the lower limb and occasionally also downwards in the upper limb. The convolutions centring around the upper part of the ascending frontal gyrus were found to be very firm at operation.

On subsequent examination of the brain the cortical region was seen to be greatly widened and contained closely packed astrocytes, with a great diminution in numbers, and upset of the normal arrangement, of the neurones. The nerve cells remaining, however, appeared normal. There were no meningeal adhesions, but it seemed probable that this gliosis was the result of an injury of which no history was obtained.

Epilepsy, arising from the premotor regions, is of the nature of *petit mal*, simple loss of consciousness and generalized convulsion with or without turning of the head and eyes to the opposite side. If the attack commences in the "frontal adversive field", the turning of the head and eye may precede the loss of consciousness. The further the lesion is placed anteriorly, the less is the tendency to strong preliminary deviation of head and eyes.

CASE V.—A man of fifty-two years had for twelve months suffered from a variety of attacks; in some a "lovely feeling" came over him for about thirty seconds. In most instances this disappeared, but occasionally he would lose the memory of the next seven to ten minutes, during which time he would apparently converse and behave rationally, but in an automatic manner. In other attacks, without warning, he would lose consciousness and fall.

Examination revealed a relative central scotoma in the left eye with an absolute paracentral scotoma in the left upper nasal field and obliteration of the left lower nasal field. The left optic disk was pale. X ray examination of the skull revealed a bony boss with a smooth upper border, apparently growing from the lesser wing of the sphenoid and projecting into the anterior and middle fossæ. At operation, Mr. Hugh Trumble exposed a large meningioma, apparently growing from the left sphenoidal ridge.

CASE VI.—Four months before his admission to hospital, to avoid colliding with a woman, a youth ran his cycle into a tree. He knows that his forehead struck the tree, but cannot "exactly" remember the moment of impact. He felt a little sick and vomited, and his right eye became rapidly swollen and blue. After walking home, three-quarters of an hour after the accident, he lost consciousness for thirty-six hours. After recovery, he suffered from occasional headaches for two months. Twelve days before his admission to hospital he felt, while shaving, sudden transient "dizziness" without any sense of rotation, and two days later he had a generalized convulsion, with biting of his tongue. He commenced to suffer from persistent right-sided frontal headache and intermittently he vomited.

Examination revealed early bilateral papilloedema and an extensor plantar response on the right side. X ray examination of the skull revealed an extensive fracture, involving both walls of the right frontal sinus. The cerebro-spinal fluid was under a pressure of 170 millimetres, and the fluid contained three lymphocytes per cubic millimetre and a protein content of 55 milligrammes per 100 cubic centimetres. A leucocyte count revealed 11,000 white cells per cubic millimetre of blood. The patient had a large abscess in the anterior part of the right frontal lobe, undoubtedly resulting from the fracture of the wall of the frontal sinus.

Parietal Lobe.

Jackson states:

The same reasoning applies, *mutatis mutandis*, to the discharge of the anatomical substrata of tactual ideas, the chief of which are impressions of surface of the fingers and adjusted movements of the hand. An epileptic discharge of the anatomical substrata of these ideas would produce numbness and spasm of the hand and arm.

The commencement of the attack demonstrates the location of the focus of discharge. If the focus is in the post-central convolution, the sensation spreads in a manner corresponding to grouping of cells in the postcentral convolution, which is similar to that in the precentral convolution. Jackson stated that the resistance to spread was less between the sensory and motor convolutions than in other directions; hence a motor convulsion was liable to end the attack.

CASE VII.—Fifteen years ago the patient first noticed a brief attack of sudden onset of a sensation of pins and needles and numbness in the thumb and index finger of the right hand. These attacks recurred at intervals, in each the sensations spreading further up the arm, until eventually the right side of the mouth became involved. At this stage, two years ago, his mouth became forcibly pulled to one side during the attacks, which then lasted

from thirty seconds to two minutes. Finally, after three such attacks in rapid succession, a fourth more severe attack occurred. After the mouth had been pulled to the right side it commenced to twitch on that side. The twitching spread to the muscles around the right eye, then to the left eye, and, finally, as it became more severe, to the left corner of the mouth. The pathological basis of this attack, apparently cortical degeneration, will be discussed later.

CASE VIII.—The patient complained of a very unpleasant sensation of pins and needles and numbness in the left thumb and index finger of ten minutes' duration. This was repeated in an hour's time, to disappear and reappear in a series of attacks of a progressively larger distribution, the hand and forearm, the arm, the left side of the lips and left side of the tongue being involved in order. In between the attacks he could use his hand relatively well, but while the numbness was present he "lost consciousness of anything in his hand"; it seemed paralysed and useless.

In this patient earlier varying epileptic phenomena were due to emboli from cardiac vegetations lodging in cerebral blood vessels. The attacks described above were probably due to a mycotic aneurysm which formed upon the left middle cerebral artery, one inch above the Sylvian fissure, and finally caused death by intracerebral rupture.

Attacks resulting from a focus further back in the parietal lobe have a most generalized sensory aura, often painful in quality; and if a motor convulsion follows, it is less likely to be localized. Foerster[4] stated that experimental stimulation of the superior lip of the interparietal sulcus in man evokes violent vertigo without movement, and this he has seen in epilepsy arising from this region.

Occipital Lobe.

As would be expected when the focus is in the receptor cells in the occipital cortex, the aura is a crude visual one, usually of coloured or uncoloured lights. If the focus is situated more anteriorly, or the process spreads, visual disorientation may be a component of the attacks.

CASE IX.—For periods of ten minutes the patient saw "flickerings of light to the side of the left eye"—rings, one or two inches in diameter, of light grey colour, opening and closing about two inches in front of his eyes. He was able to walk and talk in such attacks, but once he was surprised to find that he walked into the lintel instead of through the door. In other attacks he saw "vibrating flickering light, rather than rings", and once, when playing tennis, he found that, although he could see the balls quite well, he fumbled for them on the ground. He ceased playing, and could not find his way to the gate. Unconsciousness then supervened. Later, moving "shadows" were seen in the left field of vision. Examination revealed a left-sided homonymous lower quadrantic defect of the visual fields. At operation, Mr. Coates exposed, and removed, a small meningioma growing from the posterior part of the falx and impinging upon the anterior part of the medial surface of the right occipital lobe above the calcarine fissure.

The disorientation was explained more graphically by another patient, who stated that he wandered around knowing that he was within a stone's throw of his home, but he was quite unable to find his way there.

Temporal Lobe.

CASE X.—A boy of sixteen years had suffered for eighteen months from attacks associated with jangling noises in his left ear, flashes of light in the left field of vision and a sensation of trembling in the left arm. There was no objective movement of the arm at this stage of the attack. This aura was sometimes followed by unconsciousness; sometimes it was associated with a generalized convulsion. When examined, he had signs of raised intracranial pressures, a symmetrical defect in the left upper fields of vision, and motor and sensory signs referred to the left side of the body. At operation a cystic oligodendroglioma was found in the posterior part of the temporal lobe below the region of the right angular gyrus.

It is interesting to note that auditory hallucinations are crude; formed words are very rarely a component of epileptic attacks. Sometimes the patient refers to "a silence" as an aura of an attack.

If the focus is upon the left side in a right-handed person, inability to speak, with subsequent nominal aphasia, may be prominent in the attacks. The most interesting of all epileptic phenomena occur in lesions which, as Hughlings Jackson pointed out, involve the uncinate region.

"A paroxysm of subjective sensation of smell is an epilepsy as much as is a paroxysm of convulsion"; each is the result of sudden local discharge of grey matter.

CASE XI.—After a period of six months, during which he suffered from throbbing headache in the left side of the forehead and left temporal region, the patient commenced to suffer from "smelling" turns, in which an acrid smell commenced in the upper part of the left nostril and increased with each breath. So vague and indescribable was it that he could not be certain that it was a smell; "it may", he said, "have been a dizziness". At the same time, something flashed through his mind, usually about a person whom he had known long ago, to whom he said something which he could not remember. He could never subsequently recapture details, although he was quite certain that he had known the person a very long time ago. During these attacks consciousness of his present environment was obviously impaired, and he could be seen to lick his lips. The patient had an aneurysm of the left middle cerebral artery in the Sylvian fissure pressing upon the uncus.

In this fully developed uncinate attack gustatory and olfactory sensations, dreamy state, with "turning inwards of consciousness" and a sense of extreme familiarity are all evident. If, however, the physician waits for such a fully described attack, he will miss many instances of uncinate epilepsy. Very frequently the patient refuses to admit of an olfactory aura; but a relative will point out that the patient walked around the house endeavouring to locate the source of an unpleasant smell, of which he alone was conscious. Sometimes in an attack, otherwise resembling ordinary *petit mal*, the patient is seen to be licking his lips, champing his jaws or swallowing.

The familiarity and unfamiliarity feeling are akin to those occurring to some of us in ordinary life, and may be the basis for the strong belief in reincarnation in persons otherwise sane. The well organized "intellectual aura", with formed visual hallucinations, is of great interest, and has its anatomical counterpart in the extensive connexions of the primitive rhinencephalon. Probably it is to be correlated with the power that odours have of recalling impressions to some normal people.

The question of tonic and clonic convulsions has not been discussed. Jackson asserted that they arise at the cortical level, and it has recently been shown by electromyographic recordings that both depend upon tetanic stimulation of the muscles. Foerster explains the motor convulsion associated with frontal, parietal and temporal lesions as being due to the spread of the discharging process to neighbouring areas, which he finds are sensitive to electrical stimulation, producing "stereotyped extrapyramidal synergies"—unmodifiable flexor and extensor synergies. It has yet to be proved that these electrically excitable areas do not exert their influence through the Betz cells and the pyramidal tracts.

As an example of multiple epileptic foci, indicating an extensive cortical lesion, the next case will be described in more detail.

CASE XII.—Miss B.P., aged sixteen and a half years, stated that when she was eleven years of age she first commenced to suffer from bouts of three to seven fits, which had recurred at intervals of two to three months, and had usually been nocturnal. Her father stated that, without warning, her right elbow became flexed, with wrist and fingers extended and pronated. Her mouth then became pulled to the right and she became rigid all over. The right arm fell and generalized twitching ensued and lasted for two or three minutes. Sometimes she frothed at the mouth; occasionally she bit her tongue. She usually recovered consciousness between each fit.

Apart from these major turns, the patient described seven varieties of attacks, the details of which she clearly remembered. (i) She felt a "funny feeling in her stomach", which seemed "to come up to her throat". She could speak and knew what was going on around her. These attacks had commenced when she was eight years of age. (ii) Sometimes she felt momentarily wobbly on her legs. In these attacks, her father said, her face was flushed, and for hours afterwards she was very excitable and could not be prevented from working and rushing about. (iii) Her head and eyes turned to the right for two to three seconds and she was unable to pull them back. She "did not know anything when it was on", but did not fall over. Her father said that she stiffened and the right corner of the mouth twitched. After these attacks she sat down and played with her hands, and was obstinate and bad-tempered for some hours. (iv) Whenever she was startled, her right hand "stood up"; she illustrated the position which her father described as a prelude to the major attack. This lasted only until she "got over the fright". (v) Sometimes when she got a fright, she "lost the sense in her right hand". It felt numbed and she could not hold things in it. She flicked it about and it quickly recovered. (vi) Sometimes she saw a little white speck "in the lower part of the right eye". This lasted only for a few seconds, during which time she felt faint—as though she would have one of the third type of fits, but it never became so severe. (vii) Sometimes she did not know where anything was. She could see everything, but could not find her way about; for example, if she wished to get anything in the bathroom, she did not know for a few minutes where to go; sometimes she wandered and sometimes she just stood awaiting the return of normality.

She stated that as long as she could remember her right hand had been like anyone else's left. She wrote and did everything with her left hand, except knitting, which her mother did not know how to teach with her left hand.

Her father stated that she was a full-time baby, weighing seven and three-quarter pounds, the result of a normal pregnancy. Her doctor kindly provided an obstetric record which stated that the mother had a funnel-shaped pelvis, and the presentation was persistent occipito-posterior. The first stage of labour lasted for one hour, the membranes rupturing very early. The second stage lasted three hours, and was terminated by a very difficult rotation with forceps. The baby was in poor condition, and had a very large hæmatoma over the right parietal bone. Her mouth was distorted, the right arm was weak, and the right eye was always in the outer corner. Subsequently she always used the left hand in preference to the right, although the leg was normal. She talked before she was able to walk at eighteen months.

She had always been intelligent, but her powers of memory and concentration had been deteriorating, although no defect was detected upon examination.

Examination of the cranial nerves revealed a complete right-sided homonymous hemianopia, with sparing of the fixation point. The visual acuity was $^6/_6$ on both sides. There was slight weakness of abduction of the left eye. The right corner of the mouth moved less well than the left on voluntary and emotional movement, but associated movements were increased. Flexion movements of the right upper limb were reduced in power; especially was this marked distally. There was no detectable alteration in tone. Coordination was normal. The deep reflexes were diminished in the right upper limb, and equal in the lower limbs. The abdominal reflexes became fatigued more rapidly on the right side. The plantar responses were flexor. Superficial sensibility was normal. The appreciation of position and passive movement was much diminished in the fingers of the right hand and slightly diminished at more proximal joints. The ability to discriminate between single and double contacts was absent over the right fingers and slightly reduced over the right lower limb. Stereognosis was poor; only a rough approximation of the nature of an object placed in the right hand was possible.

The nature of the epileptic phenomena and the physical signs indicated that the patient had a large area of cerebral degeneration, maximal in the left occipital areas and extending through the parietal lobe to the precentral gyrus. It appeared that the area was too large to be capable of surgical treatment.

To elucidate the true pathological nature of the lesion air was introduced into the cerebral ventricles by the lumbar route (encephalography). The posture of the head determines whether the air enters the fourth ventricle or passes upwards into the subarachnoid space around the brain. Both lateral and third ventricles were displaced towards the left side. The anterior horn of the left ventricle was slightly larger than that of the right. The posterior part of the body of the left ventricle was greatly enlarged and displaced upwards, outwards and posteriorly, being separated from the inner table of the skull by a very small distance. The temporal horn was also greatly dilated.

The cerebro-spinal fluid was under normal pressure (level of the *cisterna magna* in the sitting posture), and was clear and colourless. It contained three lymphocytes per cubic millimetre, the total protein was 0·04%, and globulin was not increased.

There can be no doubt that the lesion was due to a birth injury causing degeneration of the nervous elements, resulting eventually in the formation of a porencephalic defect.

This patient suffered only very slight discomfort during the actual performance of the encephalography and had no subsequent symptoms. This is the criterion of a properly performed encephalography.

The Pathological Nature of Organic Lesions of the Brain which may Cause Epilepsy.

The nature of the lesion causing discharge is the next point to be considered, and from the patient's point of view it is the most important question of all. This may be already obvious in the history, and examination may shed much light upon it, but frequently this point demands the deepest thought.

Cerebral Tumours.

Cerebral tumour is the commonest cause of epilepsy commencing in middle life. Sargent[5] found that 30% of a series of 270 patients with supratentorial neoplasms, exclusive of pituitary tumours, suffered from epilepsy. Penfield finds the incidence considerably higher in his patients, particularly of the slow growing tumours (for example, meningeal fibroblastomata, 71%; astrocytomata, 84%; *glioblastoma multiforme*, 44%). The epilepsy may or may not be of localizing value.

Any form of tumour, be it neoplasm, abscess, aneurysm, gumma, tuberculoma, parasitic cyst or blood clot, may cause epilepsy.

Intracranial Aneurysms.

Intracranial aneurysms are a commoner cause of epilepsy than is realized. Two cases have been mentioned, and a third patient, having localized epileptic attacks referred to the arm, was found, upon X ray examination of the skull, to have in the expected situation an Albl's ring, due to deposits of calcium salts in the wall of the aneurysm or in the laminated clot.

Cerebral Degenerative Lesions.

Cerebral degenerative lesions are a common cause of epilepsy, and in the presenile period are commoner than is generally recognized. Such degenerations may produce signs of impairment of function, as well as of local discharge, and are exposed at operation with some frequency. There are many problems associated with such a condition. Altzheimer's and Pick's diseases are the best known, although reports are almost absent in the English literature. Both produce dementia in the presenile or senile periods, and, especially Altzheimer's disease, may produce epilepsy. In Altzheimer's disease the cerebral atrophy is usually generalized, and the histological picture is of an intense senile process, senile plaques, degeneration of nerve cells and neurofibrillary tangles being obvious. Pick's disease is characterized by circumscribed areas of cortical atrophy which may involve individual gyri, a whole lobe or several lobes together. The neurones degenerate, and there are disintegration of myelin sheaths and axis cylinders, microglial phagocytic activity, and astrocytic and connective tissue repair.

There are, however, other forms of disintegrative processes which have received no adequate description, if any at all. For this reason the following cases will be somewhat fully described:

CASE XIII.—G.H., aged thirty-six years, was admitted to the Royal Melbourne Hospital on January 2, 1936. The patient was a placid man of poor intellectual development, who gradually became irritable, excitable, antisocial and untidy during the fifteen months prior to his admission to hospital. In June, 1935, he commenced to suffer from headaches at the back of the head and neck which began during the afternoon while he was at work, and would cause him to retire to bed early. On Christmas eve he returned home, carrying his cycle on his shoulder, and said that he had had a spill. During the next day he lay on his back complaining of frontal headache and bad eyesight. After this, he was unable to read a newspaper and on January 2 he had two fits. He first complained of a bad smell, for the origin of which he made his wife search. He looked "real funny" and seemed "peculiar" for fifteen minutes, and then commenced to jerk equally on both sides of the body. Subsequent unconsciousness lasted for twenty minutes, and, when coming around, he had another similar fit in which he bit his tongue. A third attack followed on the day of his admission to hospital. He was unable to give any account of himself, and failed to recognize his wife when she visited him in hospital.

On examination, the left-sided deep reflexes were more active than the right, and the left plantar response was extensor. Owing to the mental deterioration, accurate examination was impossible. The cerebro-spinal fluid was under an initial pressure of 150 millimetres, was clear and colourless, but contained a pellicle. There were 350 lymphocytes and 25 large mononuclears per cubic millimetre. Total protein content was 0·04%. Globulin was slightly increased. The chlorides were 740 milligrammes per 100 cubic centimetres. The curve from the colloidal gold test was 0000000000. The Wassermann test gave no reaction with either blood or cerebro-spinal fluid.

The temperature varied between 38·6° and 39·4° C. (101·5° and 103° F.) for three days. He was drowsy and at times stuporous, but, if roused, was irritable and abusive. He gradually became more conscious, and at the end of six weeks was very childish and stupidly docile; for example, when told to read he lay for hours holding his book upside down. His bladder would become greatly distended before he would make any effort to micturate. The number of cells in the cerebro-spinal fluid gradually decreased to 15 lymphocytes and one large mononuclear on March 4, 1936; but the colloidal gold reaction had given a strongly paretic curve, 4555555444. On March 14, 1936, the cerebro-spinal fluid contained 11 lymphocytes and one polymorphonuclear cell. The protein was 0·07%, and the globulin fraction was increased. Chlorides were 715 milligrammes per 100 cubic centimetres. The sugar content was 0·06%. On April 9, 1936, the colloidal gold curve was 3555555441, and the Wassermann test gave no reaction. On March 24 encephalography revealed gross dilatation of the left temporal horn. Neurological examination revealed only a complete right-sided homonymous hemianopia. Periods of exaltation and continuous irrational talking, with at times great motor activity, supervened. Speech became confused, and he would repeat one phrase, such as "Collingwood, good sir", for long periods. He would demand to be kissed and was emotionally unstable, weeping at times, at times singing snatches of songs. He spent much time endeavouring to bore a hole through the wall to speak to the man next door, and at times was hallucinated and persecuted. Motor activity became uncontrollable and eventually, in an exhausted state, he died of a low-grade pneumonia.

The brain showed extreme shrinkage of the left temporal lobe, especially in its anterior part. Large venous trunks were seen running upwards over both hemispheres and converging upon the longitudinal sinus. The left Sylvian veins were greatly dilated, but were not thrombosed. Coronal sections showed that the anatomical outlines of grey and white matter had been lost in the left temporal lobe, and the superficial tissues were replaced by yellow material containing many cavities. This degenerative process was confined to the temporal lobe on the left side, and on the right side was commencing in the region of the hippocampus. The process appeared to start in the deeper layers of the grey matter.

Microscopically, there was seen to be degeneration and disappearance of nervous tissue, the tissue being in places necrosed, in others filled with lymphocytes, plasma cells and phagocytic microglial cells packed with the products of degenerated myelin. Some of the small blood vessels contained recent thrombi, but most were patent. All were surrounded by dense cuffs of lymphocytes with fat-laden cells interspersed. The pia-arachnoid in the sulci was thickened by fibrous tissue proliferation and contained many lymphocytes and dilated blood vessels.

The pathological cause of this lesion is, at present, obscure. A paretic colloidal gold curve occurs in other conditions than a syphilitic infec-

tion. The pathological process showed none of the unique changes of *dementia paralytica*; for example, the characteristic distribution of iron-staining material. Similarly, dilated veins have been seen at operation in the neighbourhood of areas of cerebral degeneration, and it is hoped that future study may solve the problem of these unusual types of lesions. The vessels do not appear to be obstructed either at operation or at autopsy.

The problem of diagnosis of such cases is also of great importance. There are no definite clinical indications; the presence of mental deterioration of a simple type in patients with focal and localizing signs without evidence of raised intracranial pressure is the usual picture. In earlier cases the intellectual deterioration may be very slight. In Pick's disease and in Altzheimer's disease the diagnosis is easier, for mental symptoms predominate, as the name presenile dementia indicates. Encephalography showing dilation of a part or the whole of a lateral ventricle may be of diagnostic value.

Case IV may be quoted as an example of a very slow degenerative process.

The patient had suffered from sensory Jacksonian attacks for fifteen years, and had no other signs or symptoms. Encephalography demonstrated unmistakable dilatation of the whole of the left lateral ventricle, particularly in its posterior part, with no displacement or distortion. The capacity of the left ventricle appeared to be at least twice that of the right. The cerebro-spinal fluid and radiological appearance of the skull were normal.

Case XIV may be an example of a localized degenerative lesion, recognized by encephalography.

The patient, a male of forty years, had for three years suffered from intermittent attacks of loss of consciousness, and once had a transient attack of sensation of pins and needles and of tingling in his right hand and forearm. The deep reflexes were constantly increased in the right arm, and the right-sided superficial abdominal reflexes were less active than those on the left. Encephalography revealed extension of the lateral part of the body of the left ventricle upwards and to the left.

In this case traction due to scarring after a forgotten injury cannot be excluded.

Causes in Early Life.

Almost equally mysterious are infantile cases of convulsions associated with loss of consciousness, from which the child emerges with or without hemiparetic signs. Without very definite pathological basis, these are usually referred to as examples of encephalitis. Some, especially those following the acute infectious diseases of childhood, are undoubtedly due to cerebral inflammation; but there are other, as yet little known, causes. Gowers asserted that many such cases were due to venous thromboses.

CASE XV.—M.C., aged eight months, was admitted to the Children's Hospital under the care of Dr. Stewart Ferguson on February 27, 1937. The parents stated that the child was healthy until 9.30 p.m. on the day of her admission to hospital, when she was being breast-fed. The left arm commenced to shake and the convulsion spread to the left side of the face and the left leg, and then became generalized. She did not recover consciousness, and twitching continued for four days, sometimes involving the left side, sometimes the right and sometimes becoming generalized. The temperature was 40·7° C. (105·4° F.) on the night of admission, and fluctuated thereafter between 39·4° and 37·8° C. (103° and 100° F.), gradually falling below normal until a terminal elevation occurred. The cerebro-spinal fluid, whether obtained by lumbar or cisternal puncture, was under increased pressure and contained red blood cells, but never more than 10 lymphocytes per cubic millimetre. The chlorides were 730 milligrammes at the onset, and gradually fell, until on April 21, 1937, the value was 622 milligrammes. No organisms were found on repeated examinations, and cultures were always sterile. On March 2, 1937, convulsions ceased, and the child remained thereafter in a state of decerebrate rigidity, tube feeding being necessary to prolong life. She died on April 5, 1937, of pneumonia.

At *post mortem* examination the cerebral hemispheres were found to be in a profound state of disintegration. Within the intact and uninflamed pia-arachnoid the brain substance appeared to be diffluent, the form of some convolutions being recognizable, but others being absent. The ventricles contained a milky fluid, which was found to contain many disintegrating microglial cells laden with products of degenerated myelin. Evacuation of this fluid was followed by collapse of the hemispheres. The cerebellum and brain stem were intact, the arteries of the circle of Willis were unobstructed. The anterior cerebral, smaller branches of the middle cerebral artery and posterior cerebral arteries were extremely small, and showed a definite arteritis with marked intimal proliferation. In some vessels recent thromboses were evident, but appeared to have just preceded death. The cortical veins, too, were extremely small, and showed intimal proliferation. The capillaries in the sections were empty or contained red blood cells which were poorly differentiated. On microscopic examination the cerebral substance was found to be completely disintegrated. No cell boundaries or nuclei could be made out, and much fatty material, stained with Scharlach R, was scattered through each section.

What pathological process beyond anæmia could determine this complete death of the cerebral hemisphere? It is hoped that these cases may be studied in connexion with future specimens and more fully described then in their pathological aspects.

This is a suitable juncture at which to deal with the known causes of epilepsy in children, and a classification of the causes of infantile cerebral palsies, which is a classification of some of the causes of epilepsy of organic origin modified from Sachs and Hausman,[6] may be given. The classification is set out in the accompanying table.

Groups.	Clinical Forms in Order of Frequency.	Morbid Lesion.
I. Paralyses of intra-uterine onset.	Diplegia. Paraplegia. Hemiplegia.	Large cerebral defects (porencephaly). Defective development of pyramidal tracts. *Agenesis corticalis.* Primary neuronal degeneration (Collier).
II. Birth palsies.	Diplegia. Paraplegia. Hemiplegia. Cerebellar form.	Meningeal hæmorrhage, rarely intracerebral hæmorrhage. Later conditions chronic meningo-encephalitis, lobar sclerosis, cysts, partial atrophies.
III. Acute (acquired forms). Diplegia.	Hemiplegia. Paraplegia. Diplegia. Choreic and athetoid disorders.	Hæmorrhage. Thrombosis (from syphilitic endarteritis and in marantic conditions). Embolism. Later conditions: Atrophy, cysts and sclerosis, chronic meningitis. Acute encephalitis.

It is probably not an over-statement to say that children with definite mental deterioration are not suffering from idiopathic epilepsy; but vascular lesions resulting from the congestion in the fits may be the cause of mental symptoms in long-standing cases. Meningitis and hydrocephalus may be added to this list as causes of epilepsy.

Hydrocephalus.—Case XVI is an example of epilepsy due to hydrocephalus.

Since the age of eight years a man of forty-eight years had suffered from epilepsy. These attacks commenced with a trembly feeling and inability to move. He shouted "catch hold of me" and then felt severe cramp in the upper anterior part of the right thigh, and the right lower limb became flexed. He then fell and lost consciousness. Otherwise he presented symptoms and signs of syringomyelia. Pathologically the spinal cord showed this condition. The cerebral ventricles, including the third and the fourth, were all dilated, apparently owing to meningeal adhesions over the roof of the fourth ventricle, binding the cerebellar tonsils to the medulla and obstructing the foramina of Magendie and Luschka.

Meningitis.—Case XVII is of interest in the development of Jacksonian motor epilepsy in the course of tuberculous meningitis.

Two and a half weeks before admission to the Royal Melbourne Hospital, a girl of nine years of age manifested a rise in temperature, felt tired and out of sorts, and was irritable, pale and drowsy. Indefinite malaise continued, and during this time she had gross pyuria. Three days before her admission to hospital she became delirious, and forty-eight hours later she had a motor convulsion commencing on the right side of the face and involving the whole of the right side of the body. She emerged with a right-sided hemiplegia and remained unconscious during her stay in hospital, with a temperature varying between 37·8° and 39·1° C. (100° and 102·5° F.), a rapid pulse (between 124 and 170) and a respiratory rate varying between 20 and 36. The right limbs were more flaccid than the left, and the deep reflexes were diminished. The right plantar response was extensor, the left equivocal. She died seven days after admission to hospital.

Lumbar puncture revealed an opalescent fluid, which developed a pellicle, under a pressure of 260 millimetres. It contained 380 lymphocytes per cubic millimetre, 0·105% of total protein with increased globulin; the chloride content was 559 milligrammes *per centum*; the sugar content was 0·045%. The colloidal gold curve was 00000013440. The Wassermann test gave no reaction. No tubercle bacilli were found in the pellicle. Two days later a cell count revealed 477 lymphocytes, 28 polymorphonuclear cells and 17 large mononuclear cells per cubic millimetre. On the next day there was a complete subarachnoid block, as revealed by Queckenstedt's test. The fluid was clear and yellow in colour, and contained 105 lymphocytes, six polymorphonuclear and two large mononuclear cells per cubic millimetre. The total protein content had risen to 0·240%. Cisternal puncture revealed a normal response to jugular compression. Microscopic examination of the urine revealed no abnormality.

The brain only was examined. The base was covered by a thick yellow membrane and tubercles were seen over the convexity, in greatest concentration near the base. The Sylvian fissures contained much exudate on both sides. On microscopic examination this exudate was seen to be composed of many tubercles, accumulations of endothelial cells, often with a perivascular arrangement, lymphocytes and polymorphonuclear cells. There were many areas of necrosis, but no giant cells could be seen. The smaller arteries revealed evidence of intimal inflammation. There was an extension of the inflammatory processes into the superficial parts of the cortex in the Sylvian fissure, shown chiefly by the presence of numbers of lymphocytes. The superficial neurones showed degenerative changes, but the deeper ones contained normal nuclei and Nissl granules, except in some areas where necrosis had resulted from obstruction of blood vessels by thromboses, the basis apparently being patches of intimal inflammation.

This process at the base of the ascending frontal convolution had apparently been the cause of epilepsy. Another feature of interest in this case which may perhaps be briefly mentioned, was the presence of ependymal tubercles.

The ependyma of the ventricles, chiefly the third and the fourth, was opaque, while elevations which on microscopic examination proved to be due to accumulation of cells of endothelial type, sometimes extended over a proliferated ependyma. Vessels in the brain tissue under these patches sometimes showed a perivascular arrangement of lymphocytes. In sections stained by Ziehl-Neelsen's method an occasional tubercle bacillus was found.

Cerebral Injury.—There may be a history of head injury preceding the onset of fits. Wagstaff[7] states that after severe war wounds not involving the dura 1·6% of patients developed epilepsy; if the dura had been penetrated, the symptom occurred in 18·7%. Penetration of the dura and the formation of a meningo-cerebral cicatrix, studied so fully by Penfield, greatly increase the liability to epilepsy. The presence of a particular type of constant headache localized to the point struck may be helpful in diagnosis. Penfield and Norcross[8] have shown that this type of headache is due to traction upon the dura by adhesions between brain and dura. Penfield[9] has shown that progressive contraction of a scar formed by astrocytes and fibroblasts, with progressive local destruction of nerve elements, constitutes cicatrization of the brain. This cicatrix, which may produce "wandering of the ventricle" towards the side of the lesion, may act as an epileptic focus. Penfield[10] has shown that excision of such a scar, extending if possible down to the ventricle, is a practical method of curing this type of epilepsy. Clean removal of cerebral tissue, leaving a space filled with cerebro-spinal fluid, is followed by little or no cicatrization.

Focal atrophy following cerebral contusion and subpial exudation of blood is not such a potent source of epilepsy, there being little or no evidence of cicatricial pull in such circumstances. It is possible that in some instances the initial injury is forgotten. Two illustrative cases may be quoted.

CASE XVIII.—The patient, a girl of nineteen years, had for five years suffered from generalized convulsions with turning of the head to the right. When two and a half years of age she fell from a garden seat on to the left side of her head. She was very shocked, and an hour later had convulsions; she later became unconscious and was unconscious for two days. When she recovered consciousness she was paralysed down the right side, but the power gradually recovered during the next two weeks. She suffered from almost continuous headache and localized pain in the left temple—a constant dull ache, sometimes increasing to a very severe stabbing pain.

Encephalography, in which distribution of air was secured over the convexity as well as in the ventricles, showed the rapid development of a subdural extra-arachnoid collection of air over the right parietal region.

Penfield has drawn attention to the importance of this in association with adhesions between dura

and brain. The patient's mother unfortunately refused to countenance an operation.

CASE XIX.—A man, thirty-six years of age, was struck, while playing football ten years ago, over the left parietal region. He was unconscious for two days and in bed for a week. From that time he has suffered from constant headache, which commences as a deep soreness over a localized part of the left parietal region and then becomes a shooting pain which passes over the left side of his head to the occipital region. As it is passing away it becomes concentrated behind the left eye. The headache is usually induced by bending down, and although it lasts for varying times, it is most frequently of short duration. During the last five years the patient has had three epileptic attacks, which commenced in each instance with a typical headache when he was milking his cows. He then felt in his right hand a sensation of pins and needles, with uselessness, which lasted for about five minutes and then disappeared, to be repeated at intervals for twenty-four hours. The sensation of pins and needles was experienced in the right lower limb only when he sat down during this period. He believes that he lost consciousness at the end of this period, but his wife says that he is conscious but irrational. He regains normality quite suddenly.

Neurological examination reveals no abnormal physical signs. By the lumbar route nine cubic centimetres of air were injected into the cerebral ventricles. The ventricles were of normal size and shape and were symmetrically disposed about the middle line. The subarachnoid space over the left cerebral hemisphere was then outlined by 40 cubic centimetres of air and the sulci appeared normal. There was no extra-arachnoid accumulation of air, although the patient was kept lying on his right side for twenty-four hours.

The patient has had only three fits during five years; and, as the encephalogram gave no positive evidence, it has been decided that no operative treatment shall be undertaken at the present time.

In traumatic cases division of adhesions between the arachnoid and dura, with excision of a cortical scar, is a practical method of treatment. Electrical stimulation of the cortex may be undertaken in an attempt to reproduce the variety of epilepsy characteristic to the patient. If such a point can be found, excision of this excitable area sometimes results in a cure of the fits.

Epilepsy may be due to intracranial extravasation of blood, and sometimes occurs in subdural hæmatomata.

CASE XX.—The patient, a male of sixty-five years, was off colour and lethargic for two weeks. Four days before his admission to the Royal Melbourne Hospital he complained of severe headache. The next day he went for a walk and was found unconscious in the Exhibition Gardens. He was taken home by tram, but, during the next forty-eight hours, had four fits. He was unconscious on admission to hospital; his systolic blood pressure was 98 and his diastolic pressure 60 millimetres of mercury. The right-sided deep reflexes were more active than those on the left, the abdominal reflexes were absent and the plantar responses were extensor. The fundi were normal, except for slight arteriosclerosis. His urine contained red blood cells, a few leucocytes and granular casts, acetone, but no albumin. The blood urea was 200 milligrammes per 100 cubic centimetres. The cerebro-spinal fluid under normal pressure contained 34 erythrocytes, one polymorphonuclear cell, four lymphocytes and one large mononuclear cell per cubic millimetre. The total protein content was 0·080%; the globulin was not increased. The Wassermann test gave no reaction. No fracture was seen in X ray films of the skull.

Fits observed in hospital commenced with deviation of the head and eyes to the right, convulsion of the right side of the face and right arm, sometimes spreading to the right leg and sometimes becoming generalized. The patient failed to recover consciousness in between convulsions and died two days after his admission to hospital. *Post mortem* examination revealed a fairly recent subdural collection of blood over the left cerebral hemisphere. Beyond sclerotic changes in the arteries, no other macroscopic or microscopic lesion was found in the brain. The kidneys showed cloudy swelling and gross sclerosis of arteries and arterioles.

Vascular Lesions.

In the elderly, vascular lesions, most usually thromboses, causing patches of cerebral degeneration, are probably the commonest cause of epileptic fits. There is no need to multiply examples of this.

The summary of a series of 130 cases studied by Fincher and Dowman,[11] in which localized or Jacksonian fits occurred, may be quoted as a summary. Cerebral neoplasm was responsible for 24·6%; trauma (accident), 20%; trauma (birth), 14·6%; post-infection, 10·7%; cerebral atrophy, 5·2%; syphilis, 5·3%; palsies of childhood, 3·8%; arteriosclerosis, 3%; undetermined, 12·2%. No evidence of increased intracranial pressure was found in 12 (37·5%) of 32 cases of neoplasm.

It is needless to stress the importance of general examination of the patient in determining the cause of a symptom which has so many causes. The occurrence of localized or generalized convulsions in cases of poisoning, during hypoglycæmic attacks, in uræmia and in coma of any description, and during Stokes-Adams attacks need only be mentioned. In one patient the finding of the bony changes of Paget's disease of the skull explained localized fits. Much judgement is necessary in deciding which cases of epilepsy are worthy of investigation. The most difficult cases are those occurring in patients who present themselves in middle life for the first time after the first fit.

Recent Studies of the Epileptic Process.

A theoretical digression may perhaps be forgiven at this stage. Some observers have stated that the cerebro-spinal fluid pressure is raised during an epileptic fit, others that it is lowered at the onset, and they adduce thereby evidence of initial spasm of cerebral blood vessels. Denny-Brown and I[12] made running records of the muscular twitching, respiration and the cerebro-spinal fluid pressure in a number of patients suffering from convulsions. The records demonstrated that changes in the cerebro-spinal fluid pressure were associated only with changes in venous pressure due to involvement of respiratory muscles in the epileptic discharge. Electromyographic records were obtained from the *tibialis anticus* muscle in a patient suffering from *epilepsia partialis continua*. Records of the contraction of *tibialis anticus* and calf muscles gave evidence of the incoordination of the epileptic discharge, flexors and extensors contracting powerfully and concurrently and producing a spasm of pain with each paroxysm. The epileptic discharge is a "discord of movement" (Gordon Holmes). The "brutal" discharge ignores the normal method of scattered stimulation of the cortical mosaic which

produces the niceties of voluntary movement. The electrical record of the discharge to the *tibialis anticus* took the form of outbursts of volleys of impulses, the resulting twitch in the muscle being of the nature of a brief motor tetanus. Voluntary movement had no effect on the discharge; during voluntary plantar flexion it continued as before, and during voluntary dorsiflexion the voluntary rhythm was superadded to the epileptic rhythm. Clonus could be elicited in the affected limb, and it was found that the epileptic discharge continued during the period of clonus. The heightened tone of the calf muscles was diminished during each twitch of the *tibialis anticus* and the rhythm of the clonus was reset by each epileptic outburst. The cortical discharge of epilepsy was therefore shown to be independent of both voluntary movement and of spinal reflexes, though they all sum their effects in the final common pathway. It is therefore reasonable to assume that voluntary and epileptic processes converge upon the Betz cells in the cerebral cortex.

During periods of post-epileptic paralysis voluntary movement may be impossible and yet the limbs may still be convulsed. It would appear that the threshold of the Betz cells is raised by a process of exhaustion of the cells, making them unavailable to weaker voluntary stimulation. The stronger "brutal" epileptic process is still able to stimulate these cells and produce a convulsion. It seems probable, therefore, that the epileptic process commences in cells higher than the Betz cells.

A method of investigating epilepsy has been introduced by Buerger, who showed that electric waves, due to activity of cortical cells, can be recorded through the intact scalp. Adrian has analysed the waves occurring in the normal subject. The waves have the greatest potential in the occipital region during closure of the eyes. Their frequency is approximately ten a second (the Buerger rhythm). They are best seen when many cortical neurones are beating together in the absence of the usual streams of afferent stimuli. This dominant rhythm is suppressed by opening of the eyes or by an attempt to solve a mathematical problem. Afferent stimulation causes some groups of cells to discharge with a higher frequency and so breaks up the rhythm which occurs when many cells pulsate with a coordinated beat. Epilepsy causes a characteristic alteration in the electroencephalogram: "an abnormal degree of association has developed and the whole cortex is a freely conducting mass" (Adrian[13]). Buerger was the first to record an epileptic fit in a human subject by this method. Gibbs, Lennox and Gibbs[14] found that a three-a-second rhythm of high voltage and spike formation of the wave, which appears to have its origin in the frontal lobe, is characteristic of *petit mal*. They found this pattern in 54 patients with *petit mal*, and never in any other condition. In the early stage of major attacks there is a relatively fast wave with a frequency of from 10 to 30 a second, which increases in voltage as the seizure proceeds. As the clonic stage appears, the waves occur in groups. In the post-convulsive period the record is either abnormally flat or, if the patient is not stuporous, large slow waves are present. They present evidence to show that the electroencephalogram may be of use in determining the site of origin of the electrical disturbances. Gibbs and Lennox have investigated epilepsy in its many aspects, but the crux of the problem always has proved elusive. As they say, a door has now been opened; whither will it lead? It seems probable that although the electrical discharge has been recorded, the essential underlying epileptic riddle is still far from solution. An advance would result if it could be shown that the process commenced elsewhere than in the cortex; but that appears improbable. The presence of acetylcholine has recently been demonstrated in sympathetic ganglia and in the basal ganglia. If it was proved that acetylcholine was responsible for the transmission of stimuli across synapses, another line of advance might be created.

Treatment.

In conclusion, a word may be said about the treatment of epilepsy for which no curative operation can be undertaken. It is important that the epileptic patient should lead as normal a life as possible and that every endeavour should be made to secure the education of the young subject. In considering medicinal treatment, the statement of Gowers is very pertinent:

> The malady is thus self-perpetuating; when one attack has occurred, whether as a result of any immediate excitant or not, others follow without any immediate cause or after some very trifling disturbance. This is due to the fact that every definite action of the nervous centres, in whatever form, leaves a disposition to the recurrence of a similar functional activity.

Because every attack facilitates the occurrence of another, the object of treatment must be to prevent the recurrence of attacks, and this can be done only by a sufficient dosage of anticonvulsant drugs, of which bromides and "Luminal" are the best. If the symptom is abolished, full dosage of these drugs should be continued for two years after the occurrence of the last attacks and then gradually withdrawn.

Acknowledgements.

It gives me pleasure to record my thanks to my colleagues on the staff of the Royal Melbourne Hospital who have so generously allowed me to examine their patients.

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THE FUNCTIONAL PATHOLOGY OF ANÆMIA.
II: THE TRANSPORT AND ELIMINATION OF CARBON DIOXIDE.[1]

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INTRODUCTION.

THE rôle of hæmoglobin is not confined to that of acting as a vehicle for the carriage of oxygen from the lungs to the tissues. Hæmoglobin is also concerned with the transport of carbon dioxide from the tissues to the lungs.

CONDITION IN WHICH CARBON DIOXIDE EXISTS IN THE BLOOD.

When blood is treated with strong acid and extracted *in vacuo*, it is found to give off some 40 to 60 volumes of carbon dioxide per 100 cubic centimetres of blood, representing the total carbon dioxide content. The solubility of carbon dioxide in blood[2] is such, however, that only 2·7 cubic centimetres will dissolve in 100 cubic centimetres of blood at body temperature (38° C.) and at the carbon dioxide pressure of alveolar air (40 millimetres of mercury). Therefore, by far the greater part of the carbon dioxide in blood must exist in combination. In what form is it combined? The fact that the carbon dioxide can be driven off by the addition of strong acid suggests that in such a reaction we are dealing with the displacement of a weaker acid from its salts by means of a stronger acid, and therefore that the carbon dioxide exists in combination with some base to form a bicarbonate or carbonate.[3] It would be an error, however, to suppose that blood behaves in respect of carbon dioxide in the same way as a simple solution of bicarbonate. This is indicated by the difference in the behaviour of blood and bicarbonate solutions in the presence of a vacuum or when subjected to different partial pressures of carbon dioxide. If a solution of sodium bicarbonate is exposed to a vacuum, it does not lose all its carbon dioxide, but only an amount which corresponds to the conversion of bicarbonate into carbonate according to the equation $2NaHCO_3 = Na_2CO_3 + CO_2 + H_2O$. Blood, on the other hand, gives up all its carbon dioxide. Similarly the dissociation curves obtained by equilibrating whole blood and sodium bicarbonate solution containing the equivalent amount of base with carbon dioxide at various pressures are quite different. The carbon dioxide dissociation curve of blood is much steeper[1][29][7] (see Figure X)

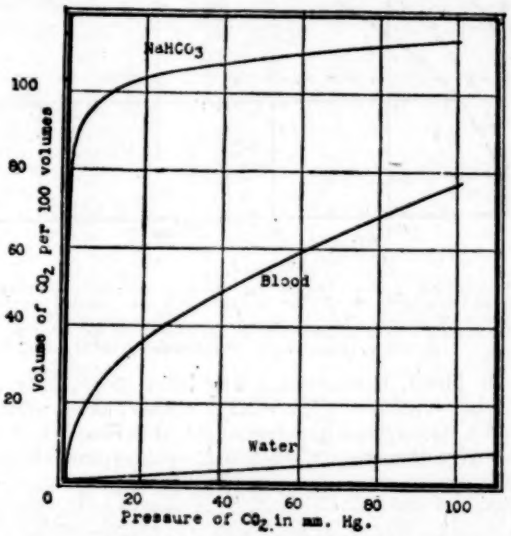


FIGURE X.

Comparison between the carbon dioxide dissociation curves of blood and of sodium bicarbonate solution of a concentration of 0·0484 N. The amounts of carbon dioxide held in physical solution in water are also shown. [After Starling, "Principles of Human Physiology", 1933, redrawn from data by Parsons (*Journal of Physiology*, Volume LIII, 1919).]

and approaches zero as the pressure of carbon dioxide becomes nil, whereas that of bicarbonate is much flatter and does not reach the base-line at zero pressure. These facts indicate that blood can take up and give off carbon dioxide much more readily than a simple solution of sodium bicarbonate, and it is obvious that the capacity to do so would be of great advantage from a physiological point of view, since but for it the power of blood to transport and eliminate carbon dioxide would be limited. The question is: what confers upon blood this peculiar property? Examination of separated plasma[1][22][23] shows that its behaviour is very like that of a bicarbonate solution: exposure to a vacuum does not cause it to liberate all its carbon dioxide, and the dissociation curve is much flatter than that of whole blood. If, on the other hand, whole blood is exposed to different pressures of carbon dioxide and then centrifuged under paraffin so as to prevent the escape of carbon dioxide, and the carbon dioxide content of the plasma is determined, it is

[1] Part I was published in the issue of August 21, 1937. Parts III and IV are to follow.

[2] At 38° C. and 760 millimetres of mercury pressure of carbon dioxide 51·1 cubic centimetres of carbon dioxide will dissolve in 100 cubic centimetres of blood. (Bohr, *loco citato*, Part I.)

[3] At the pH of the blood practically all would be present in the form of bicarbonate.

found that the dissociation curve of the true plasma,[23] that is to say, plasma which has remained in contact with the corpuscles during its exposure to carbon dioxide, is quite different from that of separated plasma, and resembles that of

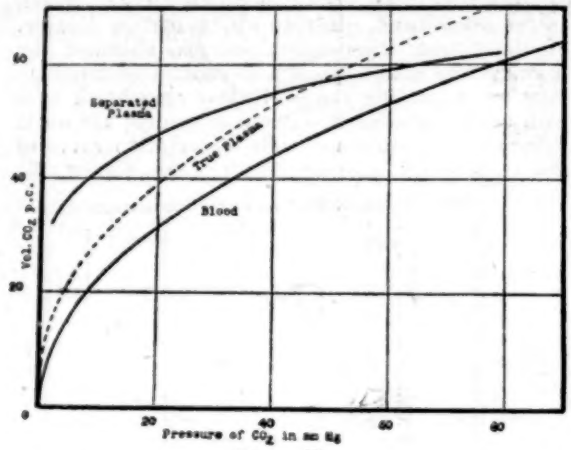


FIGURE XI.

Comparison between the carbon dioxide dissociation curves of blood and of separated plasma and true plasma from the same blood. [After Starling, "Principles of Human Physiology", 1933, redrawn from data by Joffe and Poulton (*Journal of Physiology*, Volume LIV, 1920).]

whole blood, having much the same slope, only at a higher level (see Figure XI). Clearly the presence of the corpuscles has made the difference. It is evidently the corpuscles which are responsible for

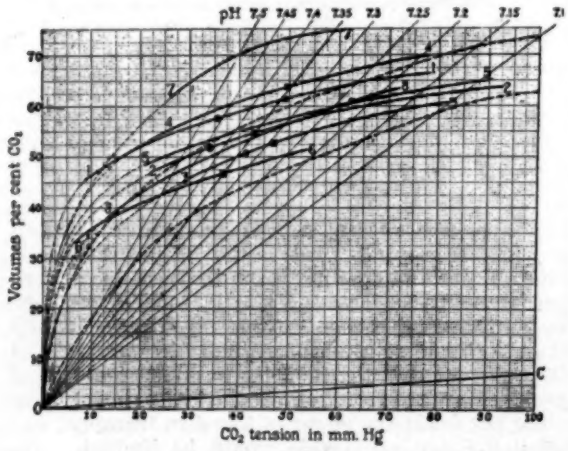


FIGURE XII.

Comparison between carbon dioxide absorption curves of blood in severe anæmia and curves of normal blood. Broken curved lines represent limits of dissociation curves from blood of normal persons, and solid curved lines represent curves from blood of anæmic patients. Straight diagonal line *O C* represents the carbon dioxide in solution and in the form of H_2CO_3. Other diagonal lines represent pH of blood. [After Barr and Peters (*Journal of Biological Chemistry*, Volume XLV, 1921).]

the behaviour of whole blood. In anæmia, in which the red blood corpuscles are diminished and there is a relative increase in plasma, the dissociation curve of blood comes to resemble more closely that of pure plasma, that is to say, it is flatter than normal (see Figure XII), which means that its capacity to take up and give off carbon dioxide for a given change of carbon dioxide pressure is diminished.[1]

Since it is to the corpuscles that we are to attribute the peculiar properties of whole blood in respect of the uptake and dissociation of carbon dioxide, the question is: how do they do this?

RÔLE OF THE RED CORPUSCLES IN THE ABSORPTION AND DISSOCIATION OF CARBON DIOXIDE.

Uptake of Carbon Dioxide.

The first light to be thrown upon this problem came from the observations of Hamburger[14][15][16] and of Zuntz[33] upon the interchange of chloride and bicarbonate ions between plasma and corpuscles when blood was exposed to carbon dioxide. These observers found that when carbon dioxide was added to blood, the bicarbonate of the plasma increased while the chloride diminished; on the other hand, the chloride of the corpuscles increased. The reverse process occurred when the carbon dioxide pressure was diminished. The exact significance of this so-called "chloride shift" has become clear with the development of knowledge regarding the chemical changes within the corpuscles and the exchange of substances between the corpuscles and the plasma during the absorption and dissociation of carbon dioxide. These are represented in Diagrams I and II and now call for consideration. The most important factors which determine the exchange of substances between corpuscles and plasma, in so far as the intrinsic mechanism of the corpuscles is concerned, are the following: (i) The capacity of hæmoglobin to combine with base or with hydrogen ions according to circumstances; also its ability to combine directly with carbon dioxide to form carbamino compounds. (ii) The action of the enzyme carbonic anhydrase. (iii) The selective permeability of the envelope of the red corpuscles, especially the impermeability of the envelope to potassium ions, in which the corpuscles are rich.

The evolution of carbon dioxide as a result of metabolic process raises the carbon dioxide tension in the tissues above that of arterial blood and, therefore, carbon dioxide diffuses from the tissues through the capillary walls into the plasma (see Diagram I). Some of the carbon dioxide in the plasma becomes hydrated to form carbonic acid according to the equation $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H + HCO_3$. But as this reaction proceeds to the right only to a slight extent in simple watery solution or even in the plasma, the amount of carbon dioxide converted into carbonic acid being only about 1%, the greater part of the carbon dioxide diffuses unchanged into the interior of the red corpuscles. Here it encounters the enzyme carbonic anhydrase,[4][3][31][28] which is capable of catalysing the above reaction. As this reaction is a readily reversible one and the position of equilibrium is not determined by the enzyme, the direction in which it proceeds will depend upon the concentra-

DIAGRAM I.

Showing the exchanges between the tissues, plasma and corpuscles during the uptake of carbon dioxide and the unloading of oxygen.

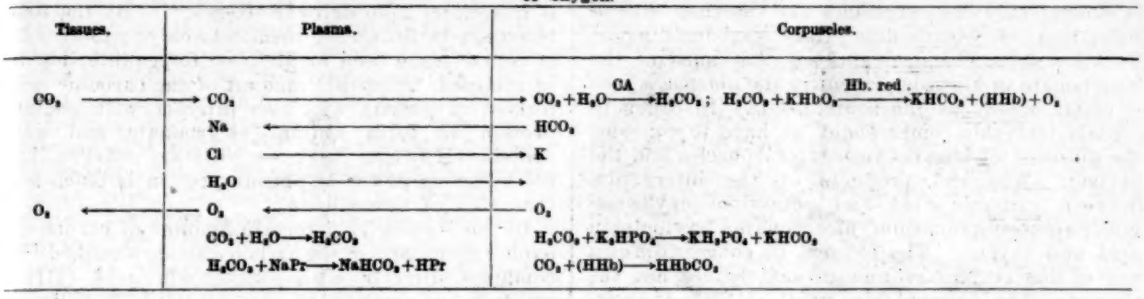
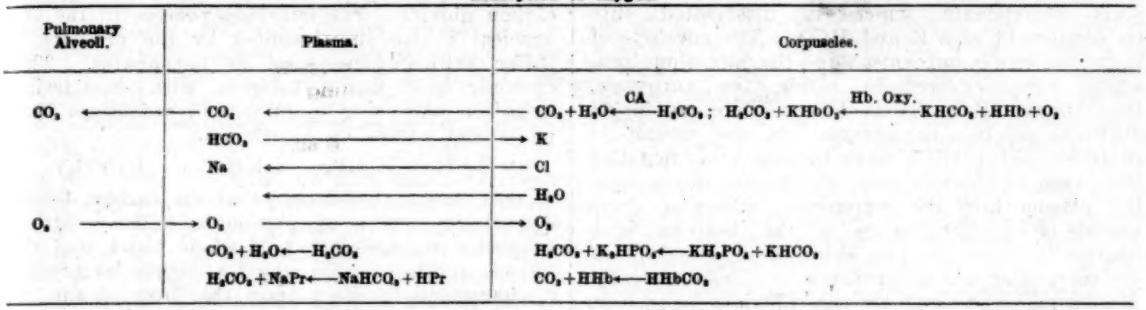


DIAGRAM II.

Showing the exchanges between the pulmonary alveoli, plasma and corpuscles during the elimination of carbon dioxide and the absorption of oxygen.



tion of the substrate (CO_2 or H_2CO_3) and the removal of one or other of the end products of the reaction. If it is to proceed to the right, therefore, there must be either an adequate rise in the concentration of carbon dioxide or a removal of H' and HCO'_3 ions or both together. In the body the rise in carbon dioxide concentration occurs as a result of the diffusion of carbon dioxide from the tissues; the removal of H' and HCO'_3 ions is due to the capacity of hæmoglobin to absorb hydrogen ions and to liberate base under certain conditions. What are these conditions? First, there is the difference in the affinity of hæmoglobin for hydrogen ions or for base, according to whether it is in the reduced or in the oxidized condition.

It has been found experimentally[7][22][9] that reduced blood is capable of absorbing more carbon dioxide than blood which is fully saturated with oxygen, and this is explained by Christiansen, Douglas and Haldane[7] and by Henderson[18] on the hypothesis that reduced hæmoglobin is more basic (a weaker acid) than oxyhæmoglobin and therefore has a greater affinity for hydrogen ions. Henderson,[18] Hill,[19][20][5] van Slyke[32] and others[17] suggest that the detachment of oxygen from the hæmatin nucleus diminishes the degree of dissociation of a particular H' ion in the nucleus, and this has the effect of increasing the affinity of the molecule for hydrogen ions. At the same time that its affinity for H' ions increases, its affinity for basic ions diminishes. The chief base which combines with hæmoglobin in the blood is potassium. In the arterial blood the hæmoglobin, being saturated with oxygen and therefore relatively acid, is combined with potassium to form an alkali salt, potassium oxyhæmoglobinate. The loss of oxygen in the capillaries causes hæmoglobin to become more basic, its affinity for potassium diminishes and that for H' increases. The potassium therefore readily unites with the HCO_3 ion of carbonic acid, while the hæmoglobin takes up the hydrogen ion to form a relatively undissociated compound, HHb (hæmoglobin acid), as may be seen from the equation

$$H_2CO_3 + KHbO_2 \rightarrow KHCO_3 + (HHb) + O_2.$$

This explains why the reaction proceeds to the right and how the end products of the previous reaction ($CO_2 + H_2O \rightarrow H_2CO_3$) are removed.

The removal of base from hæmoglobin is, however, not entirely dependent upon the changes in acidity above described. The effect of a high concentration of carbon dioxide upon the equilibrium of the reaction catalysed by carbonic anhydrase is to drive it towards the right and to give rise to the formation of an excess of carbonic acid in the corpuscles. Now both hæmoglobin and carbonic acid are weak acids, and there may not be sufficient base in the corpuscles to combine with both. Hence there occurs a competition for base, and the distribution of base will to some extent depend upon the relative concentration of the acids. An excess of carbonic acid will therefore withdraw base from hæmoglobin. The important point to notice is that hæmoglobin supplies the base which enables the blood to combine with carbonic acid to form bicarbonate. The bicarbonate which is formed in the

corpuscles is the potassium salt, since potassium is the chief base present in the corpuscles. While it is evident that the corpuscles are the chief site of formation of bicarbonate from carbon dioxide, we know from chemical analysis that most of the bicarbonate in blood is present in the plasma, where it exists chiefly as the sodium salt. In order to explain how this comes about we have to consider the diffusion of ions between the corpuscles and the plasma. The end products of the interaction between carbonic acid and potassium oxyhæmoglobinate are potassium bicarbonate, hæmoglobin acid and oxygen. The oxygen, of course, diffuses out of the corpuscles and ultimately reaches the tissues. The hæmoglobin acid (HHb) is relatively undissociated and remains within the corpuscles. We are therefore left with potassium bicarbonate which is dissociated into its component ions K and HCO_3. The envelope of the corpuscles is impermeable to the potassium ions, which therefore remain inside the corpuscle. Bicarbonate (HCO_3) ions, however, are capable of diffusing out into the plasma, but they cannot do so unless their place is taken by some other negative ions, such as chloride ions, which can diffuse from the plasma into the corpuscles; otherwise there would be a disturbance of the Donnan equilibrium[10][2] on the two sides of the envelope of the corpuscles which functions as a semipermeable membrane. Consequently chloride ions pass from the plasma into the corpuscles,[1] where they unite with potassium while bicarbonate ions diffuse into the plasma to unite with sodium. This explains the chloride and bicarbonate shift described by Hamburger and Zuntz. Owing to the diffusion of bicarbonate into the plasma, the superior buffering power and carbon dioxide carrying capacity of the red corpuscles come to be shared out with the plasma, a process known as "secondary buffering". By means of this process the carbon dioxide capacity of the plasma is brought up to that of the corpuscles and may even exceed it. We have seen that in the plasma a certain amount of carbonic acid is formed as a result of the interaction between carbon dioxide and water. Unlike ionic reactions, which are practically instantaneous, the reaction, which is a molecular one, proceeds comparatively slowly, and, as there is no carbonic anhydrase in the plasma to catalyse it, the velocity of the reaction is such that equilibrium is probably not reached for some seconds after the blood has left the capillary. The shift in pH between the arterial and the venous blood is, however, partly dependent upon the carbonic acid produced by this reaction in the plasma, the actual pH depending upon the ratio between the sodium bicarbonate and the carbonic acid $\left(\frac{NaHCO_3}{H_2CO_3}\right)$ in solution. Owing to the slowness of the reaction the change would not be complete until the blood was well on its way to the lungs in the veins, and in this way very little alteration in pH would take place in the capillaries where the blood is in contact with delicate tissues.[31] By the time blood can be drawn for chemical analysis there will, of course, have been ample time for equilibrium to be attained. A certain amount of the carbonic acid formed in plasma will also interact with sodium protein to form sodium bicarbonate and acid protein ($H_2CO_3 + NaPr \rightarrow NaHCO_3 + HPr$), but the buffering power of plasma protein is much less than that of hæmoglobin.

In the corpuscles a certain amount of carbon dioxide (about 20% of the carbon dioxide absorbed[12]) combines directly with hæmoglobin acid (HHb) to form a carbamino compound[11][25][26][28][31] ($CO_2 + HHb \rightarrow HHbCO_2$), so that hæmoglobin directly as well as indirectly acts as a vehicle for carbon dioxide. The buffering process in the corpuscles is also supplemented by the presence of buffer salts in the form of phosphates. Thus carbonic acid would interact with dipotassium hydrogen phosphate to form acid potassium phosphate and potassium bicarbonate

$$(H_2CO_3 + K_2HPO_4 \rightarrow KH_2PO_4 + KHCO_3).$$

It may be mentioned here that the carbon dioxide dissociation curve of phosphate buffer solutions somewhat resembles that of whole blood, and this affords another reason why the corpuscles produce a characteristic effect upon the form of the dissociation curve of whole blood. Although the buffering action of hæmoglobin and of salts prevents an excessive rise in hydrogen ion concentration in the corpuscles, the actual rise which takes place during the absorption of carbon dioxide is of physiological importance, as it promotes the liberation of oxygen from hæmoglobin.

Elimination of Carbon Dioxide.

Precisely the reverse changes to those above described take place in the lungs (see Diagram II). Here the fall in the carbon dioxide pressure in the plasma, due to the diffusion of carbon dioxide from the plasma into the alveoli, and the increased affinity of hæmoglobin for base consequent upon its combination with oxygen absorbed from the alveoli, are the effective factors in reversing the equilibria. The increased affinity of hæmoglobin for base causes it to withdraw potassium from potassium bicarbonate and at the same time to lose hydrogen ions. The liberated hydrogen and bicarbonate ions then unite to form carbonic acid, which in turn is converted into water and carbon dioxide under the influence of carbonic anhydrase, which now catalyses the reaction in the opposite direction to that which it did during the absorption of carbon dioxide. As the bicarbonate of the corpuscles is converted into carbon dioxide, more bicarbonate ions diffuse from the plasma into the corpuscles to replace them, and simultaneously chloride ions leave the corpuscles to enter the plasma. The capacity of hæmoglobin to absorb base is so great that in normal blood it is capable of taking up all the base from bicarbonate, so that if this process were continued, all the bicar-

[1] At the same time the rise in intracorpuscular osmotic pressure which would result from the release of basic ions from combination with hæmoglobin is prevented by the diffusion of water into the corpuscles from the plasma.

bonate in both plasma and corpuscles would be converted into carbon dioxide. This is the explanation of the fact that *in vacuo* blood can give up all its carbon dioxide. The various subsidiary reactions follow suit: the carbonic acid of the plasma diminishes owing to its conversion into carbon dioxide; and although the bicarbonate also falls, the ratio between the two when the new position of equilibrium is reached is such that the hydrogen ion concentration of the plasma falls. For reasons already given, this equilibrium is probably not attained for some seconds after the blood leaves the lungs. The fall in hydrogen ion concentration within the corpuscles has the effect of increasing the affinity of hæmoglobin for oxygen, and it therefore promotes the absorption of that gas. At the same time the carbamino compound between carbon dioxide and HHb becomes dissociated and the carbon dioxide is eliminated. The reversal of the reaction between potassium bicarbonate and acid potassium phosphate causes the formation of carbonic acid which, like that derived from the other sources mentioned, is converted into carbon dioxide and water.

In the above discussion we have been concerned chiefly with the factors which determine the direction of the changes which take place, and little has been said with regard to their velocity. The velocity factor is, however, of the greatest importance if the absorption and elimination of carbon dioxide are to take place with sufficient rapidity to meet the physiological needs of the body. In the complex chain of events which take place the velocity of the whole will be determined by that of its slowest component. Since all the changes which occur, with the exception of the chloride-bicarbonate shift, the diffusion of carbon dioxide and the hydration or dehydration of carbon dioxide, are ionic reactions and, therefore, almost instantaneous, it follows that one or other of these slower changes must be the limiting factor. Our knowledge of the rate of the two diffusion processes is incomplete, but the indication is that they are both extremely rapid. The reaction $CO_2 + H_2O \rightleftarrows H_2CO_3$, as already stated, is a molecular reaction which proceeds comparatively slowly, and in the absence of a catalyst it would certainly be the limiting factor; it probably is so even in the presence of carbonic anhydrase. In the absence of the enzyme the rate of the reaction from right to left, for example, is such that not more than 2% at most of the carbon dioxide given off in the lung could be evolved in one second, the approximate time it takes for blood to traverse the lung capillaries.[31] In order that the reaction might proceed fast enough to liberate the amount of oxygen actually given off, it would have to be accelerated at least 150 times. The factors which determine the velocity of the reaction are partly those which determine its direction through mass action; but by far the most important factor is the presence of carbonic anhydrase, and the velocity will vary with the concentration of enzyme. As carbonic anhydrase can catalyse the reaction with equal ease in either direction, it is of importance both in the absorption and the elimination of carbon dioxide.

Effect of Anæmia upon the Absorption, Transport and Elimination of Carbon Dioxide.

One effect of a diminution in the amount of hæmoglobin in the blood will be to render less potassium hæmoglobinate available to absorb hydrogen ions from carbonic acid and to give off potassium to form potassium bicarbonate when carbon dioxide is being absorbed; similarly, there will be less hæmoglobin to take up potassium ions from potassium bicarbonate when carbon dioxide is being removed from the blood. The buffering effect of hæmoglobin will therefore be diminished. This accounts for the flattening of the carbon dioxide dissociation curve in anæmia and, as already indicated, it means that the blood will combine with less carbon dioxide for a given rise in carbon dioxide pressure and will lose less for a given fall in carbon dioxide tension than normal blood. The flattening of the dissociation curve is also partly due to the loss of phosphate buffers consequent upon the diminution in the number of red cells. A further result of a diminished percentage of hæmoglobin will be a lessening of the oxygen effect upon the capacity of the blood to absorb and dissociate carbon dioxide.[30] Normally, more than 50% of the carbon dioxide carrying power of the blood is attributable to this factor. This may be seen by referring to Figure XIII.

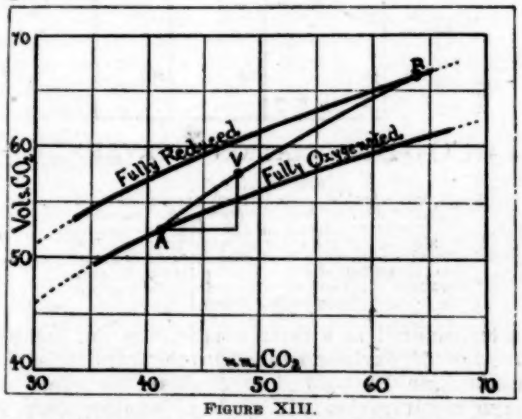


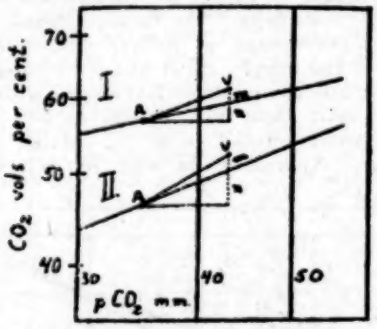
FIGURE XIII.

Dissociation curves of fully reduced and fully oxygenated human blood (only part of the curve shown). *A V B* is the physiological curve along which the carbon dioxide dissociation operates in the body. [After Starling, "Principles of Human Physiology", 1933, redrawn from Christiansen, Douglas and Haldane (slightly modified).]

It will be noted that the difference between the carbon dioxide capacity of fully oxygenated and completely reduced blood is about five volumes *per centum* at any given carbon dioxide tension; but as the blood in the body is not completely reduced, the difference between the carbon dioxide capacity of arterial and venous blood will be less than this amount. Suppose that the oxygen capacity were 18 cubic centimetres and the respiratory quotient were 0·8, corresponding to the giving off to the tissues of

6·3 cubic centimetres of oxygen and the uptake (by the blood) of 5·0 cubic centimetres of carbon dioxide. If *A* represents the point at which blood is fully saturated with oxygen at a carbon dioxide pressure of 41 millimetres, and point *V* represents the same blood having taken up five volumes of carbon dioxide, it will be seen that at least half of the increase in carbon dioxide content is due to the simultaneous reduction of the oxygen content, since a point on the curve of fully oxygenated blood immediately below would correspond to an uptake of two and a half volumes of carbon dioxide. Looked at from another standpoint, it shows that the uptake of five volumes of carbon dioxide is accomplished with a rise in carbon dioxide tension of only five millimetres, whereas to have achieved the same amount of fixation of carbon dioxide in fully oxygenated blood would have required a rise in carbon dioxide tension of about 15 millimetres of mercury.

Figure XIV shows the difference between normal and anæmic blood. The effect of a diminished percentage of hæmoglobin upon the oxygen effect is



CO_2 DISSOCIATION CURVES

FIGURE XIV.
Carbon dioxide dissociation curves plotted logarithmically. (1): curve in anæmia; (2): normal curve; *m*: increase of carbon dioxide content due to oxygen unsaturation effect; *s*: increase in carbon dioxide content due to buffer effect. [After Richards and Strauss (*Journal of Clinical Investigation*, Volume V, 1928).]

counterbalanced to a certain extent by the greater reduction of oxyhæmoglobin in the capillaries in anæmia (see Part I); nevertheless the effect of oxygen unsaturation will be less, because there is less hæmoglobin. The lessening of the oxygen effect also means that the blood will take up and dissociate less carbon dioxide for a given change in carbon dioxide tension. Not only does the diminution in hæmoglobin indirectly impair the capacity of blood to absorb carbon dioxide, but less carbon dioxide can combine directly with hæmoglobin in the form of a carbamino compound. This is another factor which limits the carbon dioxide carrying capacity of the blood.

Since the corpuscles are bearers of carbonic anhydrase, it is to be expected that a diminution in the number of corpuscles in the blood will give rise to a diminished carbonic anhydrase content. This is found to be the case.[21][24] Nevertheless, while the total amount of carbonic anhydrase per unit volume of blood is diminished, I find that the concentration of carbonic anhydrase per unit volume of corpuscles is in most forms of anæmia normal or increased (hæmolytic anæmias[24]); only after hæmorrhage and in idiopathic hypochromic anæmia has the mean corpuscular carbonic anhydrase concentration been shown to be decreased.[24] As it is the concentration of enzyme which chiefly determines the rate of the reaction; and as the reaction catalysed by carbonic anhydrase sets the pace for all the other reactions involved in the absorption and dissociation of carbon dioxide, it may be assumed that, with the possible exceptions of post-hæmorrhagic and idiopathic hypochromic anæmia, the velocity of the changes proceeding within the corpuscles in anæmia is normal or increased. Only a diminution in the mean corpuscular hæmoglobin concentration or in the mean corpuscular carbonic anhydrase concentration, or both together, might conceivably slow the reaction. We may regard each red corpuscle as a little machine in which various processes, such as the formation of bicarbonate from carbon dioxide or *vice versa*, are going forward. In anæmia each of these machines is as a rule working at a normal or increased rate; but owing to the fact that the number of machines is less than normal the total turnover per unit volume of blood per second is decreased.

One of the results of the decreased "turnover" would be the diminished rate at which bicarbonate would be produced from carbon dioxide by the corpuscles and delivered into the plasma at the periphery, that is to say, a diminution in secondary buffering. On the other hand, there would be nothing to interfere with the reaction whereby carbonic acid was produced from carbon dioxide in the plasma; indeed, the retardation of the removal of carbon dioxide from the plasma by the corpuscles would tend to cause an increase in the amount of carbonic acid so formed. The effect of these two factors—increased production of carbonic acid and diminished secondary buffering at the periphery—is to disturb the ratio $\frac{NaHCO_3}{H_2CO_3}$ on which the hydrogen ion concentration of the blood depends, in such a way as to raise the hydrogen ion concentration of the venous blood. Actually, however, the hydrogen ion concentration of the venous blood in anæmia is usually found to be about normal, because the changes at the periphery are more than offset by those taking place in the lungs. Here the carbon dioxide in the plasma would have no difficulty in escaping by a simple process of diffusion into the lung alveoli, while at the same time there would be diminished delivery of carbon dioxide from the corpuscles into the plasma. Consequently there would be a marked fall in the plasma carbon dioxide tension. The fall in the plasma carbon dioxide tension would also cause the dissolved H_2CO_3 in the plasma to be rapidly converted into carbon dioxide and water, and this, together with the retarded removal of bicarbonate from the plasma

by the corpuscles would so affect the ratio $\frac{NaHCO_3}{H_2CO_3}$ as to cause a marked fall in hydrogen ion concentration. These processes are just the reverse of those taking place at the periphery, and the one set balances the other; but they do not explain why the hydrogen ion concentration of the venous blood is normal. Direct determinations of the hydrogen ion concentration of the arterial blood show that it is below normal,[8] that is to say, there is an arterial alkalosis, and this would explain why the hydrogen ion concentration of the venous blood is normal—only the difference between the arterial and the venous pH is greater than normal. The question thus resolves itself into explaining the presence of arterial alkalosis.

Chemical analysis shows that the carbon dioxide tension in the alveolar air in anæmia is below normal, and this is attributed by Barr and Peters[1] and by Means, Bock and Woodwell[27] to overbreathing. Overbreathing and a low alveolar carbon dioxide would furnish an explanation of the arterial alkalosis. Dautrebande,[8] however, denies that overbreathing is present, and while confirming the presence of a lowered alveolar carbon dioxide and of a diminished hydrogen ion concentration in the arterial blood, he regards the arterial alkalosis as "paradoxical". Although it is claimed that the respiratory volume is normal, there is no indication as to whether the anæmic patients were compared with normal subjects or whether the same individuals were examined in the anæmic and in the normal state; nor is any information given regarding the total metabolism or the respiratory quotient. As the respiratory volume differs from individual to individual, it would be difficult, in the absence of gross variations, to say what was the normal respiratory volume in any given patient unless he was examined in the normal as well as in the diseased condition. The change in respiratory volume necessary to bring about a lowering of the alveolar carbon dioxide from the normal level (40 millimetres of mercury) to the values observed in anæmia (32 or 35 millimetres of mercury) would be quite small and within the limits of variation in respiratory volume between different individuals. Since the alveolar carbon dioxide tension depends upon the amount of carbon dioxide delivered from the blood to the lungs on the one hand, and the amount of ventilation on the other, it follows that if the amount of carbon dioxide eliminated per minute is normal or increased, as it is in most cases of anæmia, the only means of lowering the alveolar carbon dioxide would be by over-ventilation.

Dautrebande[8] and also Means, Bock and Woodwell[27] report an increase in the carbon dioxide combining power of the blood in anæmia, but the number of cases studied was very small. In a series of twenty cases of anæmia of various kinds, I[24] obtained normal values for whole blood, but when allowance was made for the change in the ratio of plasma to corpuscles (the carbon dioxide combining power of plasma is much greater than that of the corpuscles[13]) the figures corresponded to low normal or slightly subnormal values. As there is difficulty both with the uptake and dissociation of carbon dioxide in anæmia, the tissue carbon dioxide tension might be expected to show a tendency to rise. Campbell,[16] however, in experimental anæmia in the rabbit, produced by means of hæmolysis, bleeding or exposure to high oxygen

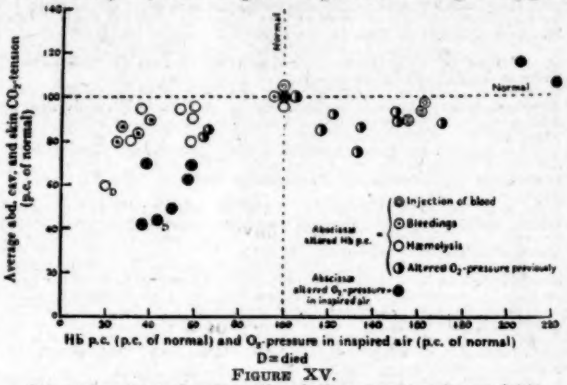

Average abd. cav. and skin CO_2-tension (p.c. of normal)
Normal
Injection of blood
Bleedings
Hæmolysis
Altered O_2-pressure previously
Hb p.c. (p.c. of normal) and O_2-pressure in inspired air (p.c. of normal)
D = died

FIGURE XV.

Composite chart showing (i) relations between hæmoglobin percentage and carbon dioxide tensions in the tissues (percentage of normal), and (ii) relations between oxygen pressures in the inspired air (percentage of normal) and carbon dioxide tensions in the tissues (percentage of normal). [After Campbell (*Journal of Physiology*, Volume LXV, 1928).]

pressures, found that the tissue carbon dioxide tension was normal or slightly subnormal (see Figure XV). It would be difficult to argue that this would also hold for the clinical anæmias in man; and no observations on the tissue carbon dioxide tension in anæmia in man have been reported. In the rabbit experiments there is no information regarding the carbon dioxide content and carbon dioxide dissociation curve of the blood or the state of the respiration, while in man data regarding tissue carbon dioxide tension are lacking. The question therefore requires further investigation, as does also the effect of exercise upon the carbon dioxide tension in the tissues in anæmia. The finding of even a normal tissue carbon dioxide tension, however, would be remarkable, as in conditions of oxygen lack due to other causes, such as the breathing of atmospheres deficient in oxygen, very low values for tissue carbon dioxide tension are obtained. In anæmia, therefore, we are dealing with a condition in which a low tissue oxygen tension may coexist with a normal (or possibly increased) carbon dioxide tension. The fact that the tissue carbon dioxide tension can remain normal in experimental anæmia, in spite of the impaired capacity of anæmic blood to absorb, transport and eliminate carbon dioxide, points to the existence of compensatory changes. These now call for consideration.

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(8) T. R. Bolam: "The Donnan Equilibria", 1932.

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DYSCHROMIA OF THE FACE, WITH A REPORT OF THREE CASES.

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DARIER defines dyschromia as "the name applied to pathological changes in the colour of the skin, resulting either from an excess or a deficiency of pigment".

An excess of pigment (hyperchromia) is much more common than a deficiency (hypochromia). Albinism is a congenital form of hypochromia; the acquired form is known as vitiligo.

The dyschromias may be localized or generalized. The latter, which include the face, and which must be taken into consideration in the diagnoses, are: the pigmentations due to Addison's disease, to pellagra, to leprosy and to tuberculosis; the pigmentary macular syphilides; the pigmentation due to arsenic; the melanodermias seen in malaria, in diabetes, in pernicious anæmia, in the cachexia of malignant disease, and often in generalized pediculosis.

The following may cause localized dyschromia of the face: (i) pigmentation due to physical and chemical causes; (ii) Riehl's melanosis, which includes Civatte's reticulated pigmentary poikilodermia, and tar melanosis, or the melanosis of Hoffmann and Habermann; (iii) chloasma; (iv) vitiligo; (v) *érythrose péribuccale pigmentaire de Brocq*.

Pigmentation due to Physical or Chemical Causes.

Exposure to sunlight and to wind produces a tanning of the face. X rays and ultra-violet rays will also produce a pigmentation. These are all temporary and gradually disappear after the cause has been removed.

Ephilides or Freckles.

Ephilides or freckles, those well-known pigmentary spots on the face, hands and forearms, appear during childhood, especially in fair or red-haired people. They are not congenital, but are hereditary in certain families. They may develop in covered parts of the body. They are much more common in the summer than in the winter, and their onset is influenced by sunlight. Matarasso recommends their removal by carbon dioxide snow; each spot is given three seconds' application. After a week, he reports, the spot desquamates and the freckles do not recur.

Goeckermann, in 1922, described two cases of a brownish-grey or slate-grey pigmentation of the face, due to face creams containing mercurous chloride. The dyschromia affected the eyelids, naso-labial folds, chin, and folds of the neck. The intensity of the pigment remained constant.

Other chemical agents may cause a persistent dyschromia. All counter-irritants and rubefacients, such as mustard plasters, tincture of iodine, chloroform *et cetera*, are liable to cause pigmentation.

Berlocque Dermatitis.

Berlocque dermatitis is the name given to a condition first described by Freund in 1916. It is a pigmentation of the face caused by the action of sunlight after eau-de-Cologne has been used. The offending agent is oil of bergamot. Other ethereal oils in toilet preparations have also been reported as causing the condition. Clinically, hanging-drop-shaped and streaked lesions are produced, which are at first erythematous and later become pigmented. The history assists in the diagnosis.

Riehl's Melanosis.

In order to disentangle the confusion arising from the term Riehl's melanosis, it is important to realize that Riehl's melanosis and Civatte's reticulated pigmentary poikilodermia are identical, and that tar melanosis differs from them only because it includes acneform lesions.

Riehl first described a case in 1917, during the War, and Civatte, in 1923, unaware of this original description, reported an identical case under a new name.

Riehl's melanosis is characterized by a pigmentary mottling of the cheeks, temples, forehead and sides of the neck, the lesions ending at the limits of the clothing. The covered parts of the body are only rarely involved. Atrophy may or may not be present, and if present it is only mild and almost indistinguishable. There is no diminution in colour on diascopic pressure. Telangiectases are present. Riehl originally thought that the sensitization of the skin was caused, during the War, either by adulterated foods, intoxication occurring through the alimentary canal, or by a vitamin deficiency. Cases have arisen since the War, however, and the above ætiological factors are doubtful.

Goldsmith states that in non-Germanic countries the term Riehl's melanosis has come to be used for cases with a known external cause, for example, tar vapour, lubricating oils *et cetera*. On the other hand, Civatte, whilst admitting that his reticulated pigmentary poikilodermia is clinically identical with Riehl's melanosis, considers that many other factors than tar, by increasing the photo-sensitiveness of the skin, will give rise to the same pigmentary changes.

Pigmentation due to coal tar, petroleum *et cetera* is a form of melanosis described in 1918 by Hoffmann and Habermann. It occurs frequently in people who work with coal or its by-products, coal tar, pitch and asphalt, and with crude petroleum. Cases have been reported from the use of impure vaseline. The symptoms are identical with Riehl's melanosis, and are accompanied by the lesions of oil acne. Not only the face, but the whole body may be affected. The colour varies from reddish-brown to black, and the pigment is "flecked, reticular or figurate". This may be accompanied by swelling, infiltration and scaling and by comedones and follicular plugging. In chronic cases there are signs of atrophy.

Hoffmann and Habermann ascribe the disease to the action of a photo-sensitizing substance closely allied to acridine. Goldsmith states that the sensitizing may be caused by the inhalation of small quantities of tar vapour or crude petroleum.

The term Riehl's melanosis, therefore, includes the pigmentation described by Civatte and by Hoffmann and Habermann. Whatever the cause, whether it be tar or petroleum, or a vitamin deficiency, or an intestinal intoxication, or whether it be unknown, all patients exhibiting the above symptoms should be classed as suffering from Riehl's melanosis.

Kinnear described a case of Riehl's melanosis due to tar, occurring in a jute spinner. He classifies these pigmentary conditions amongst the poikilodermias, and divides the five types of poikilodermia into two classes: (i) *poikilodermia vasculare atrophians* of Jacobi, which includes the poikilodermatomyositis of Petges, and (ii) Riehl's melanosis, which includes the poikilodermia of Civatte and the melanodermia of Hoffmann and Habermann.

In the second class the atrophy is of secondary importance to the pigmentation, and in fact may be entirely absent. In Riehl's first report no mention of atrophy was made.

Chloasma.

Chloasma consists of multiple irregular patches which are sharply demarcated. The colour, which varies from a yellow to a deep brown, remains constant. The pigment is unchanged under diascopic pressure. The patches are almost invariably symmetrically situated on the forehead, temples, cheeks, and at times on the eyelids and chin. An increased pigmentation about the nipples and external genitalia is often present. Chloasma has been considered to be due to various utero-ovarian changes; but it can also occur in males. Most commonly it is seen in pregnant women, and persists until menstruation starts again, but it may persist for life.

Darier considers that, as in Addison's disease, an irritation of the abdominal sympathetic nervous system together with an endocrine disturbance enters into the pathogenesis of chloasma. Goldsmith states that its prevalence in pregnant women is due to the fact that pregnancy serves only to bring it into evidence.

Poor described a form of chloasma which he called *chloasma periorale virginum*. This is characterized by pigmented macules about the mouth; these may spread to other parts of the face. These lesions appear in young virgins and may be associated with ovarian dysfunction. The condition may last for years, and often disappears spontaneously.

Vitiligo.

Vitiligo is also known as leucodermia, but it is suggested that the use of the term leucodermia should be limited to *leucodermia colli*, that form of depigmentation occurring on the neck in secondary syphilis.

Vitiligo is a depigmentation. It consists of hypochromic white patches, usually irregularly round or oval, and often symmetrical. These patches are

sharply demarcated and are surrounded by normal or hyperpigmented areas. The hypochromic areas may spread and coalesce until almost the whole body is involved. Except as regards pigment, the affected skin is not changed in any way, but it is hypersensitive to both sunlight and ultra-violet light, burning very easily and not tanning.

The prognosis in this condition is more hopeful than it used to be. Lindsay in 1929, Burgess in 1934, and Grund in 1935 have reported cures in cases treated by gold sodium thiosulphate injected intravenously, and also subcutaneously into the lesions.

Érythrose péribuccale pigmentaire de Brocq.

Ormsby and Ebert reported three cases of *érythrose péribuccale pigmentaire de Brocq*. The diagnostic feature is a diffuse brownish or brownish-red pigmentation, most marked about the mouth and extending on to the chin and along the naso-labial folds as far as the forehead. It is bilaterally symmetrical and has well-defined lateral margins. The intensity varies greatly from day to day, and even from hour to hour, but the outline of the area involved alters very little over months or years. A considerable amount of colour disappears on diascopy, but a yellowish tint remains. There are a few fine telangiectases present, and there is a more or less marked reddish tint to the skin. The sebaceous orifices are patulous.

Although closely allied to chloasma, this condition is a clinical entity. It has distinctive symptoms, the most important of which are the fluctuation of the pigment and the diminution in colour under the diascope. Almost invariably this condition has been seen in women about the menopause. Brocq considers it to be dependent on a disturbed state of the circulatory system in which dysfunction of the endocrine glands and of the gastro-intestinal system plays a rôle. This explains its extreme resistance to topical applications.

Report of Three Cases.

CASE I.—The patient, a married woman, aged forty-two years, was first seen in March, 1935. She complained of pigmentation of the face that had been present for ten weeks, and stated that this had been appearing and disappearing at irregular intervals for the last seven years. The pigmentation started as a faint brownish colour under both eyes. This would disappear for three months or more, then recur. After a few years the pigmentation gradually spread, first to the forehead and then to the face. The present attack had spread around the mouth and on to the neck, for the first time. The degree of pigmentation varied from day to day. There were no subjective symptoms.

The past history disclosed "nerve trouble" as a child, mumps, whooping cough and influenzal attacks. The patient menstruated at thirteen years of age, and then regularly every twenty-eight days until two years previously, since when menstruation had been more profuse and had occurred every twenty-one days. She had had four children. The pigmentation on the face first occurred shortly after the last child was born seven years previously.

Examination revealed dark brown irregular pigmentation under both eyes and over the bridge of the nose. The eyelids and the face immediately below both eyes were clear. Irregular light brown macules were present over both temples; the centre of the forehead was clear. Smooth, regular, light brown pigmentation was present over both cheeks and jaws, and over both sides of the neck. The edges of the coloured areas were sharply defined. The areas below the lower lip and behind both ears and the back of the neck were clear. There were discrete light brown macules on the front of the neck and covering its exposed areas. No atrophy was visible. Telangiectases were present. There was no scaliness or erythema. Diascopy caused a diminution in colour, leaving a yellowish tint.

This patient was seen again in August, 1935. For the last three months, until two days previously, the face had been perfectly clear. Then the pigmentation returned. On examination a faintly pigmented line was seen under the right eye, extending to the right ear and down the side of the neck. The areas around the mouth and the naso-labial folds were affected. Diascopy still caused a definite diminution in colour.

CASE II.—The patient, a girl, aged seventeen years, was first seen in January, 1936. She complained of pigmentation of the face of five years' duration. This did not vary in intensity, but was gradually spreading. There were no subjective symptoms. Menstruation had been delayed, but she had received treatment for this the previous year, and it was now regular, but the menstrual discharge was very dark. Otherwise the patient was quite well.

Examination revealed dark brownish macular patches of pigmentation about the mouth. Reticulated pigmentary areas, which did not disappear on diascopy, were present on both cheeks.

By June, 1936, the pigmentation had almost disappeared, and was only faintly visible. There was a faint reticular pattern over the nose and on each side of the cheeks just below the eyes.

CASE III.—The patient, a young woman, aged nineteen years, was first seen in February, 1937. She complained of dark patches on the face of six months' duration. These were constantly present and did not vary in intensity. The patches were around the mouth and there was a small patch above the right eye; the condition was not spreading. The patient's menstrual history was normal and she was in good health.

On examination, smooth, flat, brownish patches were seen on each side of the chin, just below the lower lip, on the right side of the upper lip, and just above the right eyebrow. These lesions were fixed and did not disappear on diascopy.

In Case I the outstanding features were: (i) the fluctuation of the pigment, (ii) the diminution in colour under the diascope, (iii) the age of the patient, and (iv) the symmetry and well-defined borders of the condition. Ormsby and Ebert state that the first two of these are the distinctive features in Brocq's *érythrose péribuccale pigmentaire*, and make the diagnosis from chloasma distinct. Probably most cases of this nature are diagnosed as chloasma. Although the distribution was more extensive than in similar cases previously reported, Case I was a case of Brocq's condition.

In Cases II and III we have the same type of condition. In neither case was there a history of a physical or chemical cause, nor was there any association with tar or petroleum. The lesions were not compatible with those of Riehl's melanosis or with Brocq's condition. They were, therefore, types of chloasma, and, occurring as they did in very young girls, with the main lesions around the mouth, it seems correct to say that they were cases of Poor's *chloasma periorale virginum*. Poor states that they are particularly intractable to treatment, although they often clear up spontaneously.

Both these patients were given compound ovarian tablets. The patient in Case II improved almost immediately, and after five months her pigmentation was nearly gone. So far there has been no improvement in the condition of the patient in Case III.

Pathogenesis of the Dyschromias.

Dyschromias are produced by an increase and rarely by a decrease of pigment in the skin. The cutaneous pigments are of two types, (i) melanin and (ii) hæmosiderin.

Melanin does not contain any iron, but consists mostly of sulphur combined with amino-acids. It is found intracellularly. Bruno Bloch, by means of a reagent known as dopa (dihydroxy phenylalanin), has proved that there are two types of cells containing pigment: (i) the melanoblasts or melanogens, which give a positive dopa reaction and which manufacture their own pigment, probably by means of the oxidase which they contain acting on a chromogen or propigment brought along by the circulation; and (ii) the melanophores or chromatophores, which give no dopa reaction and only store the pigment they receive. The basal cells of the epidermis and of the hair bulbs only are melanoblasts; all other pigment cells are melanophores.

Hæmosiderin contains iron. It is found in extravasated blood from hæmorrhages, petechiæ *et cetera*, and is found in the dermis only, never in the epidermis.

The stimulation of the melanoblasts to hyperactivity is the direct basis of all pigmentations. To increase the photo-sensitiveness of the skin, therefore, simply means to increase the activity of pigment formation by the melanoblasts. Exactly what causes this hyperactive formation of pigment is not known. Darier states that the hypothesis has recently been put forward that it depends on the liberation of sulphur and amino-acids, which are constituent parts of melanin, through the destruction of cells. Going further, it is now thought that the primary cause is the action of the endocrine glands, perhaps some toxic factor acting on the sympathetic nervous system affecting these glands. Consider the various pigmentary changes that are known to be associated with endocrine disturbances.

1. *The Adrenals.*—These cause Addison's disease, with its well-known pigmentation. Further, Darier states that many authors have been struck by the frequent signs of suprarenal insufficiency in melanodermia due to pediculosis, in pellagra, and in von Recklinghausen's disease.

2. *The Thyreoid.*—Goldsmith states that the frequency of pigmentary changes complicating Graves's disease is variously computed as from 3% up to 70%. In sclerodermia, which is now generally thought to be due to a dysthyreoidism, there is an almost constant cutaneous hyperchromia.

3. *The Ovaries.*—Chloasma of pregnancy and Poor's chloasma are due to ovarian disturbances. Goldsmith states that Bloch and Schrafl demonstrated the influence of ovarian hormones on pigment formation.

It is seen, therefore, that although pigmentary changes are probably due to various endocrine disturbances, the exact pathogenesis of the melanodermias is unknown. The action of the sympathetic nervous system on the endocrine glands, probably by the stimulating action of a blood toxin, is a possible explanation. This hypothesis might explain all forms of melanodermia (for example, that due to physical or chemical causes), by the destruction of cells and the resulting formation and absorption of a toxin. Riehl's melanosis might originate through a toxæmia caused by auto-intoxication, either from war-time foods, as Riehl originally suggested, or from the inhalation of tar vapours *et cetera*, or from other unknown sources of intoxication. Chloasma is agreed to be due to ovarian disturbance, and vitiligo seems to be associated with disturbance of the endocrino-sympathetic system, but, as Goldsmith says, this association is hard to define. As mentioned before, Brocq considers that his condition is dependent on a disturbed state of the circulatory system, in which dysfunction of the endocrine glands and of the gastro-intestinal system plays a rôle.

Summary.

1. The term dyschromia is defined, and the dyschromias of the face are classified into five main groups.

2. A description of each group is given, and it is shown that Riehl's melanosis, Civatte's reticulated pigmentary poikilodermia and tar melanosis are identical; but that Brocq's *érythrose péribuccale pigmentaire* is a clinical entity.

3. A report of three cases of pigmentation of the face is given. The first is diagnosed as Brocq's condition, and the other two are instances of Poor's *chloasma periorale virginum*.

4. The origin of the pigment formation is described, and the possible pathogenesis of the pigmentation is given.

Appendix.

Since the completion of this article Cornbleet has written of the connexion between vitamin *C* and pigment. He states that "since the association of vitamin *C* with the adrenal glands has been recognized it has been noted that if sufficient vitamin *C* is administered to patients suffering from Addison's disease, the hyperpigmentation is reduced to normal. The other symptoms and signs are not influenced. Another pigmentary process which has been successfully influenced by the administration of vitamin *C* is chloasma."

This opens up a fresh point of view both in the pathogenesis and in the possible treatment of these pigmentations.

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CONGENITAL SOLITARY KIDNEY, WITH A REPORT OF THREE CASES.

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The condition of congenital solitary kidney has been recognized since ancient times. Aristotle is said to have first recognized it, but the first authentic case report came from Consiliorum (1609). In 1895 Ballowitz[1] was able to collect 213 reports of cases, and in 1932 Collins,[2] in a careful review of the literature, collected reports of 572 cases, to which he added nine of his own, bringing the total to 581.

The three cases reported occurred in the writer's practice within five months—a rather unusual sequence considering the rarity of the condition.

The older anatomists regarded the condition as an anatomical curiosity of merely academic interest and paid little attention to it, and it was only when renal surgery came to be generally practised that the extreme surgical importance of congenital solitary kidney was appreciated. Tragic case reports of nephrectomies performed on the unilateral kidney stimulated interest and research into the subject. Nothing further than the recognition of its existence was achieved, however, until the introduction of the more elaborate methods of urological investigation, which enabled surgeons to make a pre-operative diagnosis with certainty; and operative calamities following its non-recognition are now seldom heard of.

There are five embryological errors which result in the development of only one functional kidney: true renal agenesia, renal aplasia, congenital renal atrophy, congenital renal hypoplasia, unilateral fused kidney.

In true renal agenesia there is complete failure of renal development on one side, and no renal tissue can be demonstrated on the side of the absent kidney. (Rare cases have been described in which the condition was bilateral.)

In renal aplasia an abortive attempt at renal development has occurred. In the renal fossa a deformed fibro-fatty mass of tissue can usually be demonstrated, which on histological examination is found to contain islands of atypical renal tissue.

Congenital renal atrophy represents a further step in development than that which occurs in aplasia. The end result of the embryological process in this case resembles renal tissue more than that found in renal aplasia, but, owing to arrest in development or to regression, a functional renal unit fails to come to maturity.

In congenital renal hypoplasia a kidney of low functional activity is formed, but it is quite incapable of carrying on adequate renal function in the event of the healthy kidney being removed or destroyed. In other words, there are two kidneys present anatomically, but physiologically there is only one.

In unilateral fused kidney, two renal units are formed, but they are fused in a cake-like or sigmoid form on one side of the body.

The first three conditions will be dealt with in this paper under the heading of congenital solitary kidney; the fourth and fifth cannot be so classed.

Some confusion as to terminology appears to exist in the literature. This seems to be due to the fact that clinicians have attempted a classification which can be made only by the pathologist. One reads, for example, of cases of congenital renal agenesia (diagnosed clinically) in which a ureter has been found to be present wholly or in part. Now the presence of a ureter indicates that the Wolffian duct has developed, and presumably the Wolffian body also, and in such cases we have no ground for assuming that some metanephric development has not occurred. Surely in such cases some "genesis" has taken place. In fact, some anatomists consider that the development of the ureteric *Anlage* acts as a stimulus to metanephric development. It is only after dissection has failed to discover any renal remnants that we are justified in using the term renal agenesia.

Similar care would be necessary in drawing a distinction between congenital renal aplasia and congenital renal atrophy. As these two conditions represent different points at which embryological development has ceased, only histological examination of the rudimentary mass could establish a diagnosis between the two. The three conditions are, however, synonymous from the point of view of the surgeon, and they are included under the heading of congenital solitary kidney.

Embryology.

In order that congenital renal agenesia, congenital renal aplasia and congenital renal atrophy may be clearly understood, it will be necessary to review the development of the kidney in some detail.

A primitive excretory organ, the pronephros, makes its appearance in the embryo at the fifteenth day as a series of mesodermal buds from the intermediate cell mass. These buds have a segmental

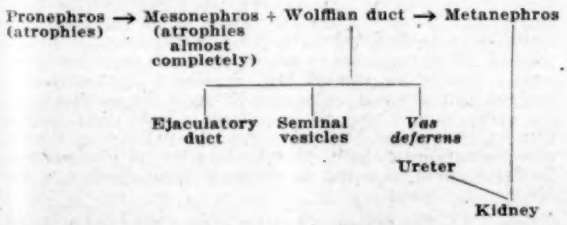
distribution and later become canalized. When fully developed, the pronephros is composed of a series of blind tubules with their free ends opening into the cœlom or general body cavity. The pronephros, after a short existence, atrophies completely.

It is succeeded by a second structure, the mesonephros. This is also developed as a series of mesodermal buds from the intermediate cell mass, which develop similarly but are more caudally situated. They become similarly canalized, and their blind ends become invaginated by tufts of blood vessels. To the medial side of the mesonephros or Wolffian body there appears a cord of cells which becomes canalized to form the Wolffian duct, and it is into this duct that the mouths of the tubules of the Wolffian body open. In certain of the fishes and amphibia this arrangement persists as the final excretory organ, but in man and the higher animals the Wolffian body atrophies almost entirely. The Wolffian duct, however, remains, and from it are developed the ejaculatory ducts, the seminal vesicles, the *vasa deferentia* and the ureter. The ureter develops as a diverticulum, which grows upwards from the Wolffian duct from the point where the latter enters the cloaca.

A third series of tubules now develops caudal to the mesonephros. This structure is known as the metanephros. The metanephros develops in a similar manner to the mesonephros. Its tubules become invaginated by tufts of blood vessels to form the future glomeruli of the kidney, and its tubules lengthen to form the secreting tubules of the kidney. While this is taking place, the diverticulum from the Wolffian duct has been growing upwards towards the developing metanephros. It invaginates the metanephros, which fits over it like a cap. From the metanephros and from the upgrowth from the Wolffian duct are formed the ureter, the kidney pelvis, and probably the collecting tubules.

Medial to the Wolffian ducts there develop two other structures: the Müllerian ducts. These fuse at their caudal ends and give origin in the female to the uterus and vagina. Their separated cephalic extremities form the Fallopian tubes. In the male the fusal caudal ends form the prostatic utricle. The Müllerian ducts are mentioned because their developmental abnormalities often run parallel with those of the Wolffian body and duct.

The accompanying diagram epitomizes the embryological process.



In such complicated development it is not difficult to understand that deviation from the normal can easily occur. The pronephros or mesonephros may fail to grow, in which case no renal tissue is developed. These two bodies may grow normally, but there may be no metanephric development, or the metanephros may commence to develop normally but may cease at any point short of complete maturity, and the point at which the embryological process ceases will determine whether agenesia, aplasia or congenital renal atrophy will be the end result.

Numerous developmental defects unassociated with the urogenital tract have been described, for example, cleft palate, hare lip, *spina bifida*, meningocele and supernumerary fingers and toes.

As would be expected, those structures derived from the Wolffian duct, the *vas deferens*, the seminal vesicles and the ejaculatory ducts, are frequently absent. The testis sometimes fails to develop. (It is developed from a ridge medial to the Wolffian body.) In the female, the uterus, vagina or Fallopian tubes are often absent or deformed. These structures are derivatives of the Müllerian ducts, which, as has been mentioned above, frequently correspond with the Wolffian ducts in their deformities.

The presence of congenital defects unassociated with the urogenital tract points to some unexplained factor which produces generally disordered growth.

Incidence.

Eisendrath,[3] from the analysis of the reports of ten writers, learned that the condition was found 85 times in 77,812 cases. Collins gives the incidence as 367, found in 337,488 necropsies. From these statistics, therefore, the incidence may be given as nearly 1 in 1,000.

Statistics vary greatly as to the sex incidence and as to the side affected. There seems to be agreement, however, that males are affected more frequently than females, and that the left kidney is absent more frequently than the right.

Pathology.

In true renal agenesia no trace of renal tissue can be found on the affected side. The renal artery is represented by a few twigs, which ramify in the retroperitoneal fat. In renal aplasia there is usually a small mass of tissue which may be connected with a fibrous cord representing the ureter. The mass contains tissue that histologically is composed of atypical renal cells. In congenital renal atrophy more typical renal tissue is found, but it is functionless. The suprarenal gland may or may not be present. The functioning kidney has been found in some cases to be ectopic.

In true agenesia the ureter is absent, which indicates, as pointed out above, that there has been absence of mesonephric development at least in the caudal part of the embryo. The fibrous cord which represents the ureter may be attached to the bladder, and may run for varying distances towards the renal fossa. This cord is in some cases canalized; and cases have been reported in which the ureter

was canalized for the whole of its length, but in which there was no renal tissue surmounting it. More frequently, however, the ureteric cord, though attached to the bladder, is represented merely by a dimple in the bladder mucosa at its attachment, or is canalized merely for a centimetre or two.

The characteristic feature of the bladder in renal agenesia is the absence of the trigone on the side of the absent kidney. The interureteric bar fades away as it approaches the position where the ureter should open into it. This, however, is not constant.

There are no symptoms attributable to the condition itself, and it is recognized only when some pathological disturbance of the other kidney calls for urological investigation. In the earlier days of surgery the anomaly frequently became evident when the only functional kidney had been removed.

Rosnohoff[4] records eleven operations — four nephrotomies and seven nephrectomies—performed on patients who had a congenital solitary kidney. In the nephrectomies death followed within periods ranging from one to nine days after operation.

The condition is quite compatible with a healthy existence. The average age of the patients in the 581 cases quoted by Collins was forty years, and the percentage of the patients who died from disease quite unrelated to the renal tract, and in whom the condition was discovered *post mortem* or in the course of a urological examination, was 68. Naturally, when pathological processes commence in the one functional kidney, or when it is injured, the prognosis becomes worse. Stewart[5] reports a case of rupture of a solitary kidney. Nephrectomy was performed and no trace of kidney tissue was found on the opposite side. Speer[6] reports a similar case *post mortem*.

Diagnosis.

From what has already been said regarding the embryology and pathology of congenital solitary kidney, the main points to be looked for in diagnosis will have been obvious. Defects and abnormalities in the genitalia discovered in a routine physical examination should arouse suspicions of some associated renal maldevelopment.

Cystoscopic and urethroscopic examination constitute the most important diagnostic procedure. Cystoscopic examination may reveal the absence of one ureteric orifice. Usually the interureteric bar fades away as it approaches the point that should be occupied by the ureteric orifice. A careful search for an atypical ureteric orifice should be made over the trigone in the mid-line, and the posterior urethra should be carefully examined. Considerable help in the location of such an abnormally implanted ureter will be gained by the intravenous injection of indigo-carmine.

The presence of two ureteric orifices does not, of course, indicate the presence of two kidneys, for, apart from those cases in which a rudimentary ureter is canalized for part of its length, there exists the curious anomaly of a single kidney with two ureters opening normally into the bladder. In all cases retrograde pyelography should be carried out as far as is practicable.

Radiology of the renal tract gives helpful confirmatory evidence. The consistent absence of a renal shadow on one side and the lack of excretion of the contrast medium in the urogram, together with the cystoscopic findings, enable the diagnosis to be made with certainty. Surgical exploration of the renal fossa to ascertain whether a kidney is present should not be necessary.

Case Histories.

CASE I.—The patient was a male aged thirty-five years. One month before I saw him he had had a severe attack of right-sided pain. The pain was situated in the right loin and was accompanied by vomiting. He became acutely ill and had great abdominal distension. Urographic examination after the acute symptoms had subsided revealed a moderate degree of hydronephrosis on the right side. There was an abrupt break at the uretero-pelvic junction. Excretion on this side was good. There was no excretion on the left side. No renal shadow was seen on the left side in any of the skiagrams. Physical examination revealed no abnormality; there were no genital defects.

Cystoscopy revealed a normal bladder mucosa and normally formed trigone. There were normal efflluxes from the right ureteric orifice, but the left was immobile. Indigo-carmine injected intravenously appeared in poor concentration from the right ureteric orifice after 15 minutes, but did not appear on the left side, although observation was continued for 30 minutes.

A catheter passed up the right ureter without obstruction, but the smallest catheter would not pass more than two centimetres up the left ureter. The pyelogram of the right side revealed a filling defect at the uretero-pelvic junction.

Pre-operative diagnosis was made of congenital solitary right kidney with obstruction by a vessel or band at the uretero-pelvic junction, or by an achalasia at this point.

At operation a normal looking, rather large kidney was found. There was an obstructing band at the uretero-pelvic junction. This was divided and the ureter and pelvis were freed. The patient's recovery was uneventful.

CASE II.—The patient was a male aged thirty-three years. He was referred for urological examination on account of right-sided abdominal pain, from which he had suffered for three months. It was not continuous or of great severity. He had some tenderness in the right loin, but firm pressure did not elicit much pain. He had no scalding or frequency of micturition. He had a chronic cough and had been treated for what was thought to be a gastric ulcer five months previously.

Slight tenderness in the right loin was found on physical examination. The patient had had a supernumerary thumb removed from the right hand twelve years previously.

A urogram revealed good secretion on the right side. The kidney pelvis and ureter were normal. No renal shadow could be seen in any of the plates on the left side. Cystoscopy showed the bladder mucosa to be normal. There was a normal right ureteric orifice. The interureteric bar was well marked on the right side, but was absent on the left. A careful search failed to reveal any left ureteric orifice, but at a point in the bladder corresponding to the position of the right ureteric orifice there was a dimple in the bladder mucosa. Indigo-carmine injected intravenously appeared in good concentration on the right side. A catheter passed to the right kidney without obstruction. Cultures from the urine were sterile. The pyelogram of the right side revealed no abnormality. No cause could be found in the renal tract to account for the patient's pain.

CASE III.—The patient was a male aged thirty-nine years. He commenced to experience pain in the right loin four years previously. The pain was confined to the loin and did not radiate. It was not constantly present, but

appeared at intervals. The attacks were accompanied by scalding and frequency of micturition (about eight times daily and three times at night). The attacks had lately become worse.

Urographic examination revealed normal excretion on the right side, but none on the left. No kidney shadow could be seen on the left side in any of the plates. No pathological condition could be seen in the right kidney. Cystoscopic examination showed the bladder mucosa to be normal. The right ureteric orifice was examined. On following the inter-ureteric ridge along, it was found to disappear into the bladder mucosa on the left side. At a point corresponding to the position of the left ureteric orifice a dimple was seen in the mucosa. A search over the trigone and posterior urethra failed to show any sign of an ectopic ureteric orifice. Indigo-carmine injected intravenously came down in good concentration from the right side.

Examination of the bladder urine revealed an occasional pus cell and one or two red blood cells. The urine was sterile on culture. Right kidney urine was found to contain one or two pus cells. It remained sterile on culture. The retrograde pyelogram was unsatisfactory. A number 11 dilating bulb passed an obstruction just beyond the uretero-vesical junction, and this was dilated to number 13 French.

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(3) D. N. Eisendrath: "Congenital Solitary Kidney", *Annals of Surgery*, Volume LXXIX, February, 1924, pages 206 to 228.

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(9) M. Moore-White: "Congenital Absence of One Kidney, with Report of Two Cases", *British Journal of Surgery*, Volume VI, December, 1934, pages 354 to 359.

(10) J. Thomson-Walker: "Genito-Urinary Surgery", pages 71 to 76.

Reports of Cases.

ARTIFICIAL PNEUMOTHORAX IN THE TREATMENT OF ACUTE PNEUMONIA.

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I HAVE had the opportunity of giving the induction of artificial pneumothorax a trial in three cases of acute pneumonia. Providing certain precautions to be mentioned later are noted, it would seem to offer a valuable aid to our treatment of this condition. In these cases it aided resolution and a quick convalescence.

Pneumonia, apart from complications such as pleurisy, empyema, pulmonary abscess or gangrene, cannot be regarded as a lung disease *per se*, but more as a severe toxæmia. Indeed, on the whole, from the point of view of treatment, the lung has been allowed to take care of itself. We have concentrated our efforts on the promotion of sleep, the aiding of the embarrassed heart, and the supply of sufficient oxygen to the patients. Providing the type of infection is known, anti-pneumococcic serum has a definite place, helping to destroy the infection and to counteract toxæmia.

In subtropical climates I have found the pneumonia jacket an unnecessary nuisance. When the skin is hot and dry, it can serve no useful purpose; when the skin is clammy with perspiration, it is unpleasant and generally in the way. Poulticing is useful for relief of pain, but I have found that it has the same drawbacks as the pneumonia jacket.

Like any other inflamed tissue, the infected lung needs rest, and it would appear from these cases that the induction of artificial pneumothorax does this in a very definite fashion.

Taylor[1] advocates the use of artificial pneumothorax in lobar pneumonia in cases seen early, within three days of onset, when consolidation is confined to one side. There must also be no complicating factor of cardio-vascular disease. By induction of artificial pneumothorax the affected lung is rested and the circulation of toxins is reduced by pressure on the pulmonary lymphatics and blood vessels. All of this must have a beneficial effect on the general condition.

Case I.

E.G., aged seventeen years, was first seen at her home on August 14, 1936, at 6 p.m. She was suffering from acute abdominal pain, chiefly on the right side, and had vomited several times. Her temperature was 39·1° C. (102·5° F.), her pulse rate was 138, and the respirations numbered 30. Abdominal disease was excluded, and physical examination of the chest revealed an area of dulness at the right base and shallow breathing. Incipient pneumonia was diagnosed and the patient was removed to hospital. At 10.30 p.m. she had a rigor with pain in the chest and elevation of temperature to 39·8° C. (103·8° F.); the pulse rate was 120 and the respirations numbered 46. Some fine crepitations had developed and the patient was in acute distress. Morphine, 0·011 gramme (one-sixth of a grain), with atropine, 0·43 milligramme (one one-hundred-and-fiftieth of a grain), was given and heat was applied.

On the morning of August 15, 1936, the patient's temperature was 39·5° C. (103·2° F.), the pulse rate was 122, and respirations numbered 50. Bronchial breathing was definite and there was some rusty sputum. There being no cardiac lesion and no infection of the other lung, I decided to induce artificial pneumothorax. Through the sixth intercostal space, in the mid-axillary line, 350 cubic centimetres of air were introduced with the greatest of ease. At 2 p.m. that day the temperature was 40·3° C. (104·6° F.), the pulse rate was 122, respirations numbered 48; the patient, however, was more comfortable and certainly did not look so ill. The temperature by evening had fallen to 39·3° C. (102·8° F.), the pulse rate was 104, and respirations numbered 32. The patient felt better and slept through the night without any sedatives.

There being no further appreciable change in the patient's condition one way or the other next morning, 350 cubic centimetres of air were again introduced. There was no reaction and the temperature fell gradually throughout the day, and at 6 p.m. it was 38·5° C. (101·4° F.), the pulse rate was 88, respirations numbered 32.

On the morning of August 17 the temperature was 38·1° C. (100·6° F.), the pulse rate was 86, and respirations numbered 30. No additional air was introduced, and as the general condition was so much better it was decided to let the lung expand.

The condition of pneumonia resolved by fairly rapid lysis, and on August 19 there was only a slight elevation of evening temperature. There was little or no expectoration, such as one expects to see in a resolving pneumonia. The patient was out of bed on August 24 and was discharged from hospital on August 30. Convalescence was exceedingly rapid.

In this case I was struck by the complete change in the patient following the induction of artificial pneumothorax, and the fact that the change was maintained. Air at each filling was introduced to a pressure just under atmospheric, as measured by the manometer on the apparatus

Case II.

R.H., a male aged twenty-four years, was brought in with a history of "flu" on October 17, 1936. On his admission to hospital his temperature was 40·1° C. (104·2° F.), his pulse rate was 110, and respirations numbered 48. He was very flushed, with some cyanosis of the lips and well-marked labial herpes. He had been ill for two days, had a frequent, sharp, shallow cough, pain below the right nipple, and was in great distress. Physical examination revealed definite signs of consolidation in the lower half of the right lung. That afternoon artificial pneumothorax was introduced through the fourth intercostal space, in the mid-axillary line, without any difficulty, and 400 cubic centimetres of air were allowed to enter.

Within three hours the patient's condition became alarming. He was cyanosed, bathed in a profuse perspiration, the pulse became weak and the temperature fell to 36·0° C. (96·8° F.). However, with the aid of stimulants his condition improved. Next morning it was evident that a definite crisis had taken place; the temperature was 37·3° C. (99·2° F.), the pulse rate was 86, respirations numbered 42. During the day the respirations dropped to 26 in the minute and there was no alteration in temperature. His general condition was excellent. No refill was considered necessary or was given. Within twenty-four hours expectoration became quite free and it was noticed to be blood-stained and muco-purulent. He continued to improve, was up on October 27, 1936, and was discharged from hospital on November 4.

I was indeed alarmed by the sudden reaction following my experience of what I would call a quick lysis with the first case. Morphine was given to this patient on his admission to hospital and was not required at any other stage of the illness.

Case III.

J.F., a male aged thirty-two years, consulted me at my surgery on October 26, 1936. He complained of rather severe pain in the left side of the chest, which caught him while breathing. It came on suddenly that afternoon. Physical examination revealed a friction rub over the base of his left lung; his temperature was 39·1° C. (102·4° F.), his pulse rate was 90, respirations numbered 32. Acute pleurisy was diagnosed, morphine, 0·016 gramme (one-quarter of a grain), with atropine, 0·43 milligramme (one one-hundred-and-fiftieth of a grain), was given at once, and he was admitted to hospital. The usual treatment for this condition was adopted. No further change was noticed until the evening of October 27, when there were definite signs of consolidation at the left base and the temperature was 40·3° C. (104·6° F.). I decided to induce artificial pneumothorax next morning. The temperature in the morning was 39·8° C. (103·8° F.), the pulse rate was 100, and respirations numbered 40. Puncture failed in the fifth intercostal space in the mid-axillary line, but was successful when tried in the sixth; 350 cubic centimetres of air were introduced. No untoward result took place; the temperature rose to 40·1° C. (104·2° F.) within two hours. It was followed that evening by a mild crisis, the temperature falling to 38·0° C. (100·5° F.), the pulse rate was 90, respirations numbered 34. Next morning the temperature was 38·4° C. (101·2° F.), the pulse rate was 88, respirations numbered 28. The patient's general condition was good and the temperature gradually fell to normal on November 1, 1936. He had no more pain in the chest, pleural or otherwise, and no additional air was introduced. Convalescence was uneventful and there was very little expectoration. He was out of bed on November 7, 1936, and was discharged on November 12, 1936.

Comment.

I have since had the opportunity of examining all three patients; they do not seem to have had any physical ill-effects from the pneumothorax. Chest expansion is good, and there is no fibrosis.

In all three cases pneumothorax was of value in bringing about a rapid amelioration of symptoms of distress, in lowering the temperature, reducing the toxæmia, and hastening recovery.

The usual nursing of pneumonia patients was carried out, Fowler beds being used. With the exception of digitalis in suitable dosage and morphine with atropine on the day of admission to hospital, no further drug treatment was used. The patients required no sedatives following collapse of the lung; pain was completely relieved and they slept well. The pneumothorax produced no symptoms *per se*.

The apparatus used was the excellent and foolproof one of Stokes and Stobo. Local infiltration of the site of puncture with 2% "Novocain" and adrenaline solution was used and the skin was nicked with a tenotome.

From a consideration of these three cases it would appear that the induction of artificial pneumothorax is of definite benefit to a patient with acute pneumonia. It gives the lung complete rest, lessens the amount of toxæmia and in general aids the *vis medicatrix naturæ*. It is, in my opinion, worth our consideration as a factor in treatment which would relieve the demand on beds in large hospitals, as well as conferring an immense blessing on those patients fortunate enough to benefit by it both physically and economically. Not all cases are suitable, however, and I shall conclude by reiterating the conditions necessary for its use: (i) the onset of pneumonia must be under three or four days; (ii) the consolidation must be confined to one lung; (iii) there must be no previous cardio-vascular disease.

Reference.

(1) B. Taylor: *The Practitioner*, Volume CXXVII, 1931, page 389.

Reviews.

THE STRUCTURE OF THE LUNG.

IT is nearly fifty years since Miller began the work the results of which are now collected in his monograph on "The Lung".[1] At that time it was believed in some quarters that there was intercommunication between the alveoli of adjacent lobules, a view which Miller's early studies seemed to confirm. He later showed that this was due to imperfections in the methods of injection and reconstruction then in use, and he succeeded in working out in detail the structure of the air passages as we now know it. Our present nomenclature of the subdivisions of the bronchial tree is to a considerable extent based on his work.

Although this work was published in 1892, its physiological significance was not realized until 1920. During the course of a controversy between the Oxford and the Copenhagen schools of physiology on the nature of the dead space of the lung, the importance of the atria in the respiratory exchange was pointed out by J. S. Haldane. Miller had been the first to describe this structure.

Miller's studies extended later to the blood vascular, lymphatic and nervous systems of the lung, and the pleura, all of which are dealt with in detail in the monograph. The subject matter is restricted to the discussion of the normal structure of the lung, and includes none of the author's work on pathological variations of structure.

An interesting historical section is given. In this the development of our knowledge of the structure of the lung is indicated by quotations from a series of works, starting with those of Vesalius, and by reproductions of original illustrations.

An extensive bibliography is included. The work is beautifully illustrated, some of the coloured figures being especially deserving of comment. The publishers are to be commended for their presentation of the work in a form worthy of the classic which it is. Those friends of Professor Miller who have made the publication possible deserve the reader's gratitude no less than the author's.

[1] "The Lung", by W. S. Miller; 1937. London: Baillière, Tindall and Cox. Royal 8vo, pp. 223, with illustrations. Price: 34s. net.

The Medical Journal of Australia

SATURDAY, AUGUST 28, 1937.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction, are invited to seek the advice of the Editor.

THE AUSTRALASIAN COLLEGE OF PHYSICIANS.

In February of this year reference was made in these pages to the formation of an Australasian College of Physicians. The establishment of this college was traced as a natural development of the Association of Physicians of Australasia, a private society, with restricted membership, but one which was conducted with enthusiasm. Emphasis was also laid on the need, in the first place, for care and watchfulness lest the activities of the new college should clash with those of the several Branches of the British Medical Association, and, in the second place, for fostering the closest possible relationship between the two bodies. It is perhaps well to repeat the statement previously made that no part of the profession, even the "senior service", can stand alone, and that the strength of every organization within the profession depends chiefly on an active and flourishing British Medical Association.

Arrangements for the legal incorporation of the Australasian College of Physicians are approaching finality. This legal process is being carried out in New South Wales because the college headquarters will be situated in Sydney. The Association of Physicians has proceeded in a leisurely fashion with the drawing up of the constitution, for its members wished, if possible, to foresee all future contingencies and to leave room for future expansion. Moreover, while the needs peculiar to Australia and New Zealand (due chiefly to geographical considerations) had to be met, the professional standards had to be kept at a high level. Sir Charles Blackburn will be the first President, and the Vice-Presidents will be Dr. S. V. Sewell, of Melbourne, Dr. C. T. C. de Crespigny, of Adelaide, and Professor Carmalt-Jones, of New Zealand. Dr. S. O. Cowen, of Melbourne, will be Chief Censor, Dr. A. S. Walker Honorary Secretary, and Dr. S. A. Smith Honorary Treasurer. The councillors are Dr. F. S. Hone, Dr. L. S. Latham, Dr. A. E. Rowden White, Dr. M. D. Silberberg, Dr. Charles Kellaway, Dr. J. G. Hayden, Dr. Konrad Hiller, Dr. A. W. Holmes à Court, Dr. H. J. Ritchie, Dr. A. H. Tebbutt, Dr. C. G. McDonald, Dr. Eustace Russell. In our previous reference to the college it was stated that land had been made available by the University of Sydney for the erection of a headquarters building. The proposal to utilize this land has been abandoned; it was realized in the first place that the cost of erecting a building that would harmonize with the architecture of the University façade would be very high, and, secondly, that the site, though admirable in all other respects, was rather far from the centre of professional life in Sydney. Trustees, acting on behalf of the college, have acquired a property, number 145 Macquarie Street, known for many years as the home of the Warrigal Club. This property is a four storied stone building, and is a good example of early colonial architecture. We understand that the structure will be altered as little as possible, though a suitable hall will be erected at the rear of the building to afford modern facilities for scientific meetings. Anyone who knows Sydney will approve of the change of situation of

the college headquarters. The Macquarie Street site is in the medical quarter of the city and close to British Medical Association House; this we hope augurs well for close cooperation between college and Association. The Government of New South Wales has given £25,000 to the building fund and has generously allowed the gift to be applied to the altered plan; for this the Council of the college is most grateful. It is also grateful to many who have made gifts to the college and have given promises of financial help. The building is to be chiefly a New South Wales responsibility. Moneys from other States will be devoted to an endowment fund, which, augmented by dues from members, will be used to defray working expenses, to found scholarships for medical research, and to establish and maintain a library. (As far as the library is concerned, there must be no overlapping with other libraries; but that is a subject which must be left for consideration on another occasion.)

Medical practitioners outside the college have asked what purpose it will serve. The college will be an examining body and will provide a uniform higher qualification in medicine for practitioners in Australia and New Zealand. At the present time the requirements for doctorates in medicine in the universities of Australia and New Zealand are by no means uniform, and there seems to be little chance of obtaining uniformity. The time is not far distant when every member of the staff of a large hospital will be required to have a higher qualification in the special branch of medicine that he proposes to practise. The college will not only act as a stimulus for the attainment of higher degrees, but will indirectly raise the standard of the practice of internal medicine, particularly in institutions. Doubtless it will carry on the tradition of the Association of Physicians in the advancement of internal medicine and the promotion of friendship amongst physicians. Finally, the college will, we trust, maintain itself as a scientific body and eschew medical politics; this is the province of the British Medical Association, the only body that can speak for the whole company of medical practitioners.

Current Comment.

SYPHILITIC EPILEPSY.

EPILEPSY is essentially a disease of early life, but cases are encountered which have originated in adult, middle or even later life. These cases are indistinguishable from the ordinary epilepsy of early age. Convulsions occur in neurosyphilis which cannot be differentiated from epilepsy. W. L. Bruetsch and M. A. Bahr give full accounts of five cases of what they describe as syphilitic epilepsy.[1] They quote Krüger as stating that epileptiform seizures occur in about one-quarter of general paralytic patients who remain untreated. They state also that, occasionally, epileptiform attacks are observed in persons with meningovascular syphilis, who have hemiplegia or other organic disturbance and in whom the convulsion is only an additional manifestation of a well-defined entity. The term syphilitic epilepsy, however, is reserved for convulsive seizures which resemble idiopathic epilepsy in all respects and which leave no sign of organic brain disease after the attack. The differentiation from idiopathic epilepsy may be extremely difficult or even impossible. W. M. Dedman and H. J. Morgan, in an analysis of cases of neurosyphilis at the Vanderbilt University Hospital over a period of seven years, found only five cases among 335 patients. In one of the five cases antisyphilitic measures apparently put an end to the convulsive seizures. E. A. Walker, in 1936, stressed the importance of syphilis as a factor in determining epilepsy commencing in adult life.

Bruetsch and Bahr state that anatomical examinations of the brains of sufferers from syphilitic epilepsy are almost lacking. The patients described by them were observed over a period of ten years and their convulsive attacks were identical with those of essential epilepsy. In every one of them the seizures began in or after middle life. Two of them had, in addition, chronic verrucose endocarditis. In the first case the brain lesions consisted of a large area of cortical necrosis in the left supraorbital region and of small areas of cystic degeneration in the cortex of the central and temporal convolutions. In the meninges there was diffuse syphilitic fibrosis over the anterior two-thirds of the upper aspect. The areas of degeneration were due to syphilitic endarteritic vascular changes which were not numerous. Microscopic cortical areas of necrosis filled with scavenger cells were present. This patient had been injured in a railway wreck many years previously, but this was excluded as causing residual traumatic changes giving rise to the cortical areas of degeneration. In the second case autopsy revealed chronic syphilitic meningitis and gross cortical defects in the left parieto-occipital area and in the right temporal lobe. A supravital examination of the brain cortex

[1] *American Journal of Syphilis, Gonorrhœa and Venereal Diseases*, May, 1937.

showed endarteritic changes in the capillaries. In some necrotic areas of the cortex there were numerous scavenger cells, filled with pigment and *débris*, suggesting that some of the lesions were recent. In the third case atherosclerosis of the basilar arteries and small cystic areas in the basal ganglia were present, but no gross changes in the cortex were apparent. Histological investigation of the brain revealed endarteritic changes in the capillaries. Microscopic areas of softening were seen about vessels in the layer of Betz cells of the central convolutions with a few scavenger cells. In some of the larger cerebral vessels there were endarteritic changes with lymphocytic infiltrations which were more suggestive of syphilis than of arteriosclerosis. The fourth and fifth cases showed verrucose endocarditis. In the fourth case the brain exhibited a diffuse fibrosis of the pia-arachnoid over the anterior two-thirds of the hemispheres and small brownish areas of cortical necrosis in the temporal lobes. Microscopic investigation showed the areas of cortical necrosis to depend on vessels having characteristic appearances of syphilitic endarteritis. In this case serological investigation revealed no abnormality. The diagnosis did not seem to have been established beyond doubt. In the last case histological examination revealed in the vessels of the cortex and meninges syphilitic changes in the form of endarteritis, producing, in some cases, complete obstruction of the lumen. In this case, however, the convulsions actually followed a fall from a bicycle. Cerebral trauma accordingly had to be considered, but Bruetsch and Bahr considered that the lesions were characteristic of active cerebral syphilis of the meningovascular type and not traumatic.

These pathological investigations do not bring to light anything that will explain the epileptic seizures and there were too many complicating factors to render them explicit. Bruetsch and Bahr, however, claim that, in all five cases, the syphilitic nature of the brain lesions could be demonstrated. In one of the series, in which the first attack occurred when the patient was sixty-seven years of age, there were additional arteriosclerotic changes. In three instances there was a history of trauma to the head, which may have determined epilepsy. The brain changes, however, in the patients here recorded did not indicate that they were residual lesions of a former injury. In those with verrucose endocarditis it is possible that the changes were rheumatic, and in rheumatic fever lesions have been described closely resembling syphilitic endocarditis. The pathological findings in all the five cases were characteristic of the meningovascular type of neurosyphilis. Bruetsch and Bahr state that not all persons react with a convulsive disorder to the type of cerebral involvement occurring in these patients. In the Central State Hospital of Indianapolis are syphilitic brains with lesions in the same cortical areas, but the patients did not have epileptic attacks. Cobb has stated that, of patients with known brain trauma, only 4% have seizures, and that of patients with brain tumours only 21% to 30% have convulsions. Cobb and Spiegel rather favour the idea that, in addition to cerebral injury, there must be a constitutional factor in people who have seizures after destruction of brain tissue. Hence of syphilitic patients with identical brain lesions, some have convulsions and some do not.

The cases reported by Breutsch and Bahr have been described in some detail on account of the interesting paper by Dr. Graeme Robertson and the Victorian Branch discussion that are published in this issue. The subject is one of extraordinary difficulty, and, although Breutsch and Bahr's contentions may not carry conviction, they show that neurosyphilis should in certain circumstances be suspected as a cause of convulsive seizures.

CARBOHYDRATE METABOLISM.

THE more prosperous inhabitants of Bengal and other parts of India seem to be particularly liable to *diabetes mellitus* in middle life. Their food consists mainly of carbohydrate, including a large quantity of sugar, and is poor in animal protein and some vitamins. G. Sankaran and K. Rajagopal fed twelve rats with a diet resembling this, in an attempt to produce *diabetes mellitus* experimentally.[1] The diet contained raw polished rice (50%), white flour (10%), sugar (12%), mustard oil (8%), ghee (3%), milk (3%), grams (5%), fish (5%), root vegetables (2%), leafy vegetables (2%), and condiments in small quantities. The animals did not thrive, and some died earlier than would normally have been expected. Ten were alive at the end of eleven months, three after fourteen months, and two only after sixteen months. Presumably this high rate of mortality was due to avitaminosis. After eleven months it was noted that the blood sugar content of the fasting animal was on the average actually lower than normal; no evidence of diminished glucose tolerance was observed. Examination of the pancreas of the two rats that survived for sixteen months was made by Dr. Radhakrishna Rao. He was unable to detect any changes in the islets of Langerhans. Sankaran and Rajagopal mention that Hrubetz recently reported an unsuccessful attempt to produce "idiopathic diabetes" in rats by feeding them with a stock diet supplemented by 25% of sucrose. Hrubetz did not perform glucose tolerance tests.

It is possible that the high carbohydrate diet taken by Indians and people of some other races is not responsible for any high incidence of *diabetes mellitus* among them. It may be that the disease is more apparent because of their persistence in taking excessive amounts of carbohydrate when their insulin-producing mechanism is failing. At the same time, it is conceivable that the islets of Langerhans might become exhausted and might subsequently degenerate as a result of overwork. The administration of large quantities of carbohydrate to rats, though they be in thousands, will not provide a solution.

[1] *The Indian Journal of Medical Research*, April, 1937.

Abstracts from Current Medical Literature.

PÆDIATRICS.

Plasma Phosphatase and Rickets.

NOAH MORRIS *et alii* (*Archives of Disease in Childhood*, February, 1937) have investigated the significance of plasma phosphatase in the diagnosis and prognosis of rickets. They point out that ordinary clinical examination suffices for the diagnosis of moderate degrees of rickets; but something more is necessary for the detection of milder forms of the disease when the metabolic disturbances are not sufficiently great, or have not continued long enough to produce clinical manifestations. Skiagrams have been used to great advantage as an aid to diagnosis, but several drawbacks are associated with their employment. Their interpretation is difficult in mild forms of the disease, and in many cases it is not possible to determine whether any healing is taking place until a series of at least three skiagrams, taken at weekly intervals, are available. Chemical examination of the blood has also been undertaken. The serum calcium does not alter greatly in uncomplicated rickets, but a reduction of inorganic phosphorus has long been used as a valuable indication of the presence of rickets. Freudenberg, however, has pointed out that a low serum phosphorus is not pathognomonic of rickets, since it may occur in pneumonia and other acute infections, muscular dystrophies, myxœdema and cœliac disease. Hess and others have also shown that sometimes the phosphorus content of the serum may be normal, even when there are definite clinical manifestations of active rickets. The product of the calcium and phosphorus values of the serum has for some time been accepted by many as a valuable index of the rhachitic process, a product above forty indicating a healing and one below thirty an active stage; but the significance of this has been disputed. In attempting to assess the value of plasma phosphatase as a diagnostic test for rickets, and also as a means of determining the presence and rate of healing, the authors have based their results on the examination of five hundred and six infants and children in the first two years of life, who either had manifest rickets or might possibly have been suffering from the effects of vitamin *D* insufficiency. In 84% of the cases with clinical and X ray evidence of rickets the plasma phosphatase was increased above normal limits. It is suggested that a rise in plasma phosphatase is an earlier manifestation of the rhachitic state than that provided by ordinary clinical or radiographic examination. The level of the phosphatase cannot be taken as an index of the severity of the rhachitic process in the individual patient. A moderate degree of correlation was observed between the phosphatase rise and the fall in phosphorus and calcium phosphorus product, especially the last mentioned. It would appear that of the three, an increase in plasma phosphorus is the most delicate test of the rhachitic state. In untreated active rickets the plasma phosphatase continues to rise, and the administration of vitamin *D* prevents this rise, and in two or three weeks causes a fall. It is suggested that the phosphatase is increased whenever the supply of calcium is unable to meet the demand of the bone cells as a result of defective intake of minerals or vitamin *D*.

Vincent's Stomatitis as a Cause of Obscure Fever.

HOWARD L. EBER (*Archives of Pediatrics*, March, 1937) draws attention to the possibility of the occurrence of prolonged low-grade fevers in children due to undiagnosed mild Vincent's stomatitis. Many of these cases may be overlooked if the gums are not carefully examined as a routine measure. There is acute inflammation of the gums, with redness, œdema, and a fine chalk-like membrane, producing an appearance as if talc had been scattered over a reddened gum. The condition often succeeds some acute infection, from which the patient recovers, but which is followed by a persistent slight rise of temperature. The children are listless and refuse food, and have more evidence of toxæmia than apparent clinical findings would indicate. The treatment is extremely simple. For older children, undiluted hydrogen peroxide is effective, used four or more times daily as a mouth wash. A soft tooth-brush dipped in a compound of five parts of potassium chlorate, ten parts of sodium perborate, and boroglycerin to make 60 parts, and applied to the teeth and gums every four hours, brings about a very rapid cure. In addition to the specific action of sodium perborate on the Vincent's organism, the compound reduces the œdema and relieves the inflammation of the gums. Farrell and McNichols have drawn attention to the use of undiluted hydrogen peroxide as a prime factor in curing Vincent's angina, and they feel that the use of arsenical preparations is not justified. The author is entirely in accord with this opinion in the treatment of the mild cases. When ulceration with induration is present, intravenous injections of neoarsphenamine may be of value.

Gold Tribromide in the Treatment of Pertussis.

J. EPSTEIN (*Archives of Pediatrics*, March, 1937) comments upon the large clinical experience showing the undoubted value of the gold tribromide treatment of pertussis, introduced by him a few years ago. He gives a brief report of 250 patients thus treated, and of 100 patients as controls treated with the usual antipertussis remedies, consisting chiefly of sodium bromide, antipyrin, phenobarbital, camphorated tincture of opium and pertussis vaccine. From a comparison of the therapeutic results it is evident that gold tribromide is of decided therapeutic value in the treatment of whooping cough. Under gold treatment the average duration of the cough in 250 cases was three to eight weeks, while under the drug, vaccine and placebo treatments the average duration of the cough in 100 cases was ten weeks. It was also found that the gold treatment was of great value in relieving the violence and frequency of the coughing seizures and in giving the children considerable rest and sleep. In the group of 100 children there were 19 who received prophylactic vaccination, and this treatment did not have any material effect on the course of the disease. In the author's experience, preventive vaccination of pertussis is of doubtful value. Attention is drawn to the fact that gold tribromide is an unstable and easily oxidized chemical, and that it consequently undergoes deterioration and decomposition when dispensed in pills, capsules or aqueous solution. It is best made up in a stable, assayed and palatable elixir known as "Elixir Bromaurate". The average dose for children is a teaspoonful every four hours.

ORTHOPÆDIC SURGERY.

Fracture-Dislocations of the Cervical Vertebræ.

W. CONE AND W. G. TURNER (*Journal of Bone and Joint Surgery*, July, 1937) discuss the treatment of fracture-dislocations of the cervical vertebræ by skeletal traction and fusion. In the past four years they have had under their care 36 patients with such injury, and in 12 of these the skeletal muscular and ligamentous involvement was such that operative intervention and fusion were carried out with satisfactory end-results. The absence of spinal cord symptoms after trauma to this region in some cases makes it easy to fail to appreciate the significance of injury to these parts and later to find deformity that might have been avoided by early spinal fusion. They describe cases in which pieces of bone were taken from the ilium, the tibia or a rib, and in each instance were tied to the cervical vertebræ as two parallel grafts with fine Babcock rustless steel wire. When a long time has elapsed since the injury, with development of late deformities and advancing spinal cord involvement, they consider spinal fusion an operation of necessity, and find immobilization of the neck by skeletal traction on the operating table of great assistance. It is practically always necessary to rongeur away the articular facets which are preventing reduction; reduction then tends to occur spontaneously, provided skeletal traction is maintained. The authors describe an apparatus for maintaining skeletal traction, either by means of special tongs or by rust-

less steel wire inserted through holes in the skull. As soon as the wound permits, plaster fixation of the head, neck and torso is employed and skeletal traction removed in order to get the patient up. Plaster immobilization should be maintained for six months.

Early Protected Weight-Bearing in Fractures of Leg, Foot and Ankle.

F. B. GURD (*Surgery, Gynecology and Obstetrics*, June, 1937) enumerates the untoward complications and sequelæ following fractures below the knee as: (i) delayed union or, in unusual cases, non-union; (ii) prolongation or permanence of interference with joint function; (iii) contractures and consequent interference with the action of muscles and tendons; (iv) circulatory disturbance; (v) pain upon weight-bearing due to decalcification of bone and ligamentous structures. Since 1918 he has treated all fractures of the leg below the knee by immobilization in plaster, great care being taken to see that no constricting bands exist, and that there are no dead spaces beneath it, the plaster being carefully moulded about the malleoli and to the upper end of the tibia before it is set. In every instance he has found the procedure of value in permitting return to work after a few days. He applies a stirrup of plaster around the heel and lower portion of the leg to reinforce the plaster cast, and has devised various boots which may be applied over the plaster cast and so obviate the use of the Böhler iron. He believes that earlier union occurs, associated with the more perfect return of function, and that even in a fracture of both bones of the legs the patient may return to substantially full duty within less than a month.

Tuberculosis of the Knee Joint.

S. TREGUBOW (*Journal of Bone and Joint Surgery*, July, 1937) states that many authors have recorded a large number of cases of tuberculosis of the knee joint treated with success by operation. In contrast to their former attempts to remove as much as possible of the bone that appears to be affected, it now becomes their aim to create an ankylosis in the position of election. Careful post-operative immobilization is of great importance, and its recognition has produced increasingly better results. The author has performed 109 resections since 1921, with good results in 77%. Generally speaking, the section of the bone is done in such a way that the least amount of shortening is produced, and very few surgeons resort to fixation by clamps or metal wire. A position of slight flexion is desirable, great care being taken to avoid the position of *genu recurvatum*. The majority of surgeons do not leave either a drain or a tampon in the wound. Immobilization is secured by a plaster bandage applied to the limb from the foot to the pelvis. The period of immobilization varies from three to six months. The author permits his patients to walk on crutches and bear weight slightly on the affected leg about six weeks after operation; after another six weeks the plaster bandage is shortened or replaced by a new one, which does not encircle the pelvis. The second bandage is worn for about three months. During this period free weight-bearing is allowed. A removable bandage made of plaster and gelatine or gelatine and formalin is applied at the end of this time, and the time during which it is worn is governed by the firmness of the ankylosis. Adolescence and maturity are the most suitable ages for operation, although excellent results have been obtained in old age, and resection may be successfully performed on patients between the ages of ten and fourteen years if care is taken not to injure the epiphyseal cartilages. The best time to perform an operation for ankylosis is the period of abatement of the process. The operation should be a simple one, aimed chiefly at the formation of ankylosis, bone foci being thoroughly curetted and filled with bone chips.

Prevention and Treatment of Ununited Fractures.

VARIOUS speakers (*Proceedings of the Royal Society of Medicine*, June, 1937) discuss the records of cases of non-union at many hospitals in England during the past ten years. A. M. A. Moore selected 65 cases of non-union in which the patients were treated as in-patients, and in which the fracture was of at least six months' duration. He obtained no results of positive value from complete blood investigation, and felt that the frequent examination of the part by X rays could not be blamed for non-union. Surgical intervention, such as the plating of a fracture, was primarily responsible for non-union in 13 out of 19 cases. He is of the opinion that whilst skeletal traction is an extremely valuable method of applying extension, it is responsible for non-union by permitting over-extension. In the case of phalanges unsatisfactory immobilization appeared to be responsible for non-union in this series. H. H. Fairbank considers that the causes of non-union are local and not general. Imperfect immobilization is the chief cause, but want of apposition of fragments and deficient blood supply of one of them are of importance. The too early use of massage, too early movement of adjacent joints, treatment of a simple fracture by internal fixation without providing adequate external splintage, malposition of fragments and skeletal traction are all causes of non-union. He expresses the opinion that open operation, which should give something near perfection in its results in 100% of cases, should be resorted to more frequently. Functional use of the limb, even to the extent of weight-bearing, if this can be done without risking immobilization, undoubtedly saves many patients from operation. The only exception to this rule is the case in which some angular displacement persists. Bone grafting is an essential part of the operation for real non-union, and the inlay graft is considered the best type; but the intramedullary insertion of one fragment is often beneficial. In non-union of the femur he is accustomed to apply a plate and at least eight screws in addition to the graft. G. R. Girdlestone lays great emphasis on the importance of damage to the circulation of the bone as a cause of delayed union and non-union. In ununited fracture of the femur, union may occur as a result of reestablishment of circulation after the patient has been walking by the aid of an appliance for some months; but if it does not then occur, bone grafting may be carried out under more favourable conditions. In grafting in such cases he avoids the complete stripping up of the bone ends in order to avoid damaging the circulation, and has found that his results have improved since following this course. He prefers a combination of inlay, osteo-periosteal and multiple small chip grafts. K. H. Pridie considers that the healing time of fractures varies inversely with the cross section of the bone at the site of fracture. Investigation of the ununited fractures sent to the Bristol Clinic for treatment disclosed over-traction to be the most common cause of non-union. In treatment for non-union he simply employs multiple drilling of the bone ends, using a high speed electric drill and providing adequate splintage. St. J. D. Buxton found union occurred in 20 cases of non-union in infants treated by a slide graft from the same tibia. The fibula was invariably divided and a bridge of bone left at the distal end of the proximal fragment to help firm fixation of the graft, which was an essential part of the operation. B. W. Howell concludes that the best results in the treatment of non-union are obtained by open operation, extensive stripping of the periosteum up and down the shaft, freshening of the bone ends, and the insertion of a long, wide, massive autogenous bone graft within the periosteum.

Endothelioma of Tibia.

ARTHUR E. PORRITT (*Proceedings of the Royal Society of Medicine*, April, 1937) reports a case of endothelioma of the tibia. The patient, aged thirty-seven years, was a diabetic. There was a hot, slightly tender, fluctuant swelling occupying the middle third of the subcutaneous border of the tibia. X ray examination revealed bone erosion and some new bone formation, due to either osteitis or atypical Ewing's sarcoma. At operation the greatly thickened periosteum was incised and an irregular cavity cleaned out. Histological examination revealed slight evidence only of bone destruction; the diagnosis was between endothelioma and chronic infection with much histiocyte formation. Deep X ray therapy was administered. Fracture occurred later; but the condition improved, and generous callus formation occurred.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at the Medical Society Hall, East Melbourne, on June 2, 1937, DR. F. KINGSLEY NORRIS, the Honorary Secretary, in the chair.

Epilepsy.

DR. E. GRAEME ROBERTSON read a paper entitled: "Epilepsy as a Symptom of Organic Lesions of the Brain" (see page 331).

DR. W. J. GRIEVE congratulated Dr. Graeme Robertson on his most interesting, instructive and stimulating paper. He said that in opening the discussion he wished to confine his remarks to the epilepsies of childhood. He emphasized the great importance of a careful initial history and routine examination in order to exclude (*a*) symptomatic convulsions and (*b*) organic lesions of the central nervous system.

Dr. Grieve then reviewed symptomatic convulsions excluding the obvious causes and placed them into the following groups: (*a*) The febrile group. In this group one had to emphasize the frequency of acute tonsillitis as a cause of infantile convulsions, also *otitis media* and other infections. (*b*) A group that was possibly reflex. Probably in this group there already was a predisposition to convulsions, and slight irritating factors such as teething, worms and intestinal infections were sufficient to precipitate an attack of convulsions. (*c*) A metabolic group. This group included the convulsions of nephritis (acute and chronic), hypoglycæmia and calcium deficiency. As regards hypoglycæmia, Dr. Grieve had been interested in a child with diabetes who had developed hypoglycæmia, who had had convulsions, and who was left with persistent hemiplegia. Calcium deficiencies were most common between the ages of six months and two years, and occasionally were a complication of rickets and cœliac diseases *et cetera*. Tetany occasionally occurred in this group.

Dr. Grieve then discussed the diseases of the central nervous system producing convulsions, and excluded the obvious acute infections. In this group, tumour of the brain was an occasional cause of recurrent convulsions in childhood. When convulsions occurred, the tumour frequently was supratentorial, but occasionally the increased infratentorial pressure and the internal hydrocephalus produced by an infraventricular growth would be sufficient to precipitate convulsions.

Dr. Grieve indicated the relative infrequency of supratentorial tumour in childhood and felt that tumour was an infrequent cause of convulsions.

Congenital syphilis occasionally caused convulsions and it was always necessary to look for the stigmata of this disease. Nowadays syphilitic involvement of the central nervous system in childhood was rather infrequent and could be easily overlooked.

Dr. Grieve also reviewed the organic and degenerative cerebral lesions which had been discussed by Dr. Graeme Robertson. They proved a most interesting group and probably were responsible for at least 25% of the epilepsies in childhood. Dr. Grieve thought that encephalography would probably increase the percentage of this and decrease that of the idiopathic group. He referred to the work done recently at the Royal Aberdeen Hospital for Children, where a series of children with mental defects *et cetera* were investigated by encephalography. It would appear that in a limited number of specially selected patients encephalography might be helpful in diagnosis, prognosis and treatment.

Dr. Grieve then discussed the differential diagnosis and drew attention to the following conditions: organic cerebral lesions, already mentioned; congenital syphilis; syncope, especially in older children; masturbation in female infants; breath-holding in small children and hysteria in older children.

Dr. Grieve reviewed the onset of epilepsy in childhood. He stated that in all epilepsies the period between fourteen and sixteen years was the most frequent age of onset, but that in childhood the first three years were the most usual age. One-eighth of all cases of epilepsy occurred at this age and 50% to 60% of epilepsy in childhood. Another slight increase occurred at the seventh and eighth years, the period of second dentition. Attacks of *petit mal* almost invariably were epileptic and only a small percentage of children with infantile convulsions subsequently developed epilepsy.

Discussing ætiology, Dr. Grieve said that he thought there was an essential predisposition to epilepsy in a large percentage of the epilepsy of childhood. He indicated the importance of heredity, for in the investigation of the histories neuropathic tendencies or epilepsy were found to be very common on one or other side.

A large number of epilepsies commenced in the first few months, and Professor Still had repeatedly drawn attention to the periods of special stress in a child's life; for example, birth, the first dentition, the second dentition and puberty. There was no question but that at these periods the onset of epilepsy or exacerbations seemed to be common.

Dr. Grieve dealt with the so-called reflex causes, such as tonsils and adenoids, and gastro-intestinal upsets, which played a small part in the production of idiopathic epilepsy. He thought that they might be contributing factors only, and he had seen several patients who were temporarily very much worse after removal of tonsils and adenoids, although it is more common to find the patients improve for some time, but not permanently.

Dr. Grieve again indicated the frequency of organic cerebral lesions of a degenerative type as a cause of epileptic convulsions. He reviewed the period of the second dentition in which other nervous manifestations, such as habit spasm, night terrors and nocturnal enuresis, occurred.

Dr. Grieve referred to the articles written by Wilkins in the *Journal of Pædiatrics* of March, 1937. In these articles 254 non-institutional epileptic children were reviewed. Wilkins divided these epileptics into three groups. Those in Group I, with an intelligence quotient of over 80 and no apparent neurological lesions, numbered 111 or 43·7%. Those in Group II, with an intelligence quotient below 80 with no apparent neurological lesions, numbered 82 or 32·3%. Those in Group III with definite neurological lesions numbered 61 or 24%. This classification was of interest, for the prognosis was materially affected by the absence of organic cerebral lesions and a good intelligence quotient.

Dr. Grieve pointed out that, although *petit mal* was very infrequent in adults with epilepsy, it was very much more frequent in children and was very easy to overlook. The attacks were often very frequent and were usually resistant to treatment. The term was frequently used loosely, for it often included attacks which were minor motor attacks and it would seem better to reserve the term for true *petit mal*, in which no motor manifestations apart from some twitching of the eyelids occurred. The prognosis of *petit mal* was guarded, for the mentality of the patients was frequently affected, especially if the attacks commenced in the first year. There was a better prognosis for *petit mal* if the onset of the attacks occurred in older children.

Before leaving the question of *petit mal*, Dr. Grieve reviewed the condition of pyknolepsy. He had had an opportunity of observing several patients with this condition. He felt that it was extremely rare, but that nevertheless it was a definite entity. He reviewed the characteristic features, such as the age of onset—four to ten years—the absence of any mental change, the very frequent daily attacks with no motor manifestations, the long continuance for months or even years, the sudden cessation and the lack of response to drugs.

Dr. Grieve then discussed nocturnal epilepsy and stated that it often occurred when the child was getting off to sleep or was in the waking state. He frequently had found

long intervals occurring between attacks of nocturnal epilepsy and had thought that the prognosis in this particular type of epilepsy was rather better than in other varieties. He thought that occasionally incontinence of urine occurring at night was an indication of nocturnal epilepsy, and he thought that this factor should be kept in mind in children who developed this condition.

Dr. Grieve then referred to the question of localized attacks of epilepsy. In his experience tumour was only a very occasional cause and he felt that a large proportion was due to local atrophic degenerative conditions, although he appreciated the fact that in many no neurological lesions were discoverable on clinical examination. He thought that encephalograms might be of particular value in this variety of attack. In a proportion of cases after a localized attack of epilepsy a temporary local paresis was present, and he referred to the temporary paresis that occasionally followed ordinary simple infantile convulsions. Congenital syphilis also was an occasional cause of a localized Jacksonian attack.

Dr. Grieve then discussed the epilepsies of childhood in relation to the mental condition of the child affected. This, of course, was one of the most serious aspects of the epilepsies of childhood and he thought that the age of onset of the epilepsy was a very important factor, for the prognosis was extremely bad if the onset occurred within the first two years. After the age of two years the mentality was often modified and the child drifted into the typical epileptic mental state, which Dr. Adey would subsequently describe.

The variety of epilepsy undoubtedly played a part in the prognosis from the mental standpoint, and Dr. Grieve indicated the bad prognosis in children when *petit mal* attacks occurred in the first year. He felt that in older children the presence of *petit mal* attacks was not such a bad prognostic omen. The clinical demonstration of a neurological lesion undoubtedly made the prognosis worse.

Dr. Grieve then referred to the conclusions drawn by Wilkins in the articles previously referred to, on the occurrence of remissions in the epilepsies of childhood. Dr. Wilkins's conclusions were that long remissions were frequent in patients suffering from major attacks only, for he had found that 23% of the patients reviewed had remissions for one year or more, and 19% had remissions for two years or more. He had found the remissions more frequent in patients with a normal intelligence quotient. He had found that remissions were infrequent in patients with *petit mal* attacks and in patients under two years of age, and had found remissions rare if the disease had existed for longer than five years.

Dr. Grieve then summarized the good features as regards prognosis: (i) Normal intelligence; (ii) number and frequency of attacks, for example, intervals between attacks longer than one month and total number of attacks less than ten; (iii) response to treatment.

In reviewing the prognosis of these patients, Dr. Grieve indicated the necessity for a long period of observation, for many patients had very long remissions during adolescence. Usually a nine years' remission was looked on as being indicative of cessation of the attacks, but in a number even longer periods had occurred and attacks had recommenced. He did not think that one should be too gloomy about the prognosis in children, for probably about 10% of epileptics made complete recoveries. The most hopeful period of onset from the standpoint of prognosis was that of middle childhood. If the onset occurred after the age of three years and the attacks persisted, there was a very big possibility of the mentality being modified. If the onset was before three years, probably definite mental changes would supervene. The prognosis as regards *petit mal* attacks had been indicated previously.

Dr. Grieve then briefly summarized the position as regards treatment, and indicated the importance of attending to the general health of the patient and modifying his mode of life. He thought that companionship and the discipline of games were helpful and that the teaching of various handicrafts was of definite value. Of course occupations and games which would be associated with danger to the epileptic during attacks would have to be very closely supervised.

Dr. Grieve then discussed the drug treatment and emphasized the importance of regular and continuous administration of the drugs selected. He thought that treatment should be continued for eighteen months to two years from the time of the last attack.

As regards dosage, he felt that the adequate smallest dose was the ideal and indicated that the time of administration also was important. This, of course, would depend on the time at which the attacks usually occurred; for example, if they were nocturnal attacks, a large dose of sedative should be administered at bedtime.

Dr. Grieve thought that bromide still had a definite place in the drug treatment, and in children the dose should vary from 15 to 60 grains per day, depending on the severity and frequency of the attacks and the age of the patient. He often combined bromide and sodium biborate, giving half as much biborate as bromide. Chloral in relatively large doses was undoubtedly useful for infantile convulsions and for the frequent *petit mal* attacks which occurred in the first year. Phenobarbital was an efficient drug and could be used by itself, or the soluble salt could be combined with bromide. He used one-half to two grains of phenobarbital in twenty-four hours. Occasionally tincture of belladonna was added with benefit to the above mixture. Dr. Grieve was of the opinion that the belladonna was of most use in the *petit mal* attacks.

As regards the ketogenic diet, Dr. Grieve's experience had been very limited. He had found it extremely difficult to maintain an effective ketogenic diet in children. It was easy to do this at hospital, but difficult to maintain after the patient left hospital. He thought that it had a definite place and should be tried in some of the more intractable cases, especially in *petit mal*, but in his own experience the improvement manifested had not been sustained.

DR. J. K. ADEY said that the epileptic temperament had long been recognized by psychiatrists. These patients were noted for their extreme egocentricity. They were self-assured and thought that what they did must be right, and they looked upon it as a personal insult when people disagreed with them. They were easily upset, and to pass them without saying "good-morning" caused them to be offended for the rest of the day. Combined with these characteristics, they were frequently hyper-religious; but their religion, too, was of a selfish nature, and was inclined to be centred on themselves. In passing it was of interest to note the fact that Swedenborg, Mahomet, and possibly St. Paul, all religious reformers, were epileptic. Dr. Adey said that no religious reformer could carry conviction to others if he was not absolutely convinced himself of the truth of his statements. He went on to say that epileptics gradually became restricted in their outlook on life, ceasing to take interest at first in the general news of the world, then in their families and immediate surroundings; finally an epileptic would be concerned with himself alone.

Dr. Adey said that there was also another side to the epileptic temperament. These patients had their virtues. They were not lazy and would work hard and long for very little reward, some praise occasionally going a long way with them. With epileptics in hospital it was noticed that they were kind and considerate to other patients, particularly to other epileptics. It was well recognized that epileptics were happier in company with others suffering from the same disease. For this reason every large mental hospital had special wards for epileptics only. Work was good for them and they should not be stopped from doing some; it helped to prevent the progress towards complete egocentricity. They were particularly inclined to become irritable before a fit and were difficult to manage by their relatives. People should be told to leave them alone when they were irritable. They did not want soothing, but should be encouraged to go to bed and no one should be allowed to go near them. Although it was indisputable that there was an hereditary factor in epilepsy, it was on very rare occasions that it was manifested among brothers and sisters in the same family.

Dr. Adey concluded by referring briefly to treatment. He had found that some patients were improved if they were given "Luminal sodium" in solution instead of in tablet form. This was inconvenient to use in hospital out-patient work because the "Luminal sodium" did not keep well for more than eight days in solution. It was, of course, very dangerous for a confirmed epileptic to cease taking "Luminal", even for twenty-four hours, as this might precipitate an attack of epileptic furor or of *status epilepticus*. For the latter condition, Dr. Adey had found injections of Bayer's preparation, "Luminal 20 per cent", very satisfactory.

DR. THOMAS RYAN briefly recounted the history of a boy whose attacks of *petit mal* ceased abruptly after an operation for undescended testis.

DR. GUY SPRINGTHORPE congratulated Dr. Graeme Robertson on the excellence of his paper and the feat of memory which he had exhibited in the description of the clinical details concerning so many patients. Dr. Springthorpe asked for an opinion as to the relationship of focal sepsis to epilepsy. In his experience the views on this matter which he had noted seemed vague and conflicting.

DR. H. F. MAUDSLEY drew the attention of the Branch to an advertisement advocating the use of South African snake venom as a cure for epilepsy. He would like to know if any favourable results had been recorded. The laity had been bitten by the idea. He was satisfied that local venin gave absolutely negative results. The advertisement seemed so good that some close inquiries were warranted.

DR. W. W. OSTERMEYER said that he possessed a book by Gowers which was forty-five years old. It was a book about the dynamics of life. Disease had its dynamics and one of these was epilepsy. Something seemed to pull a trigger and a reserve of energy was released. He wondered at times why *petit mal* and *grand mal* were grouped together. In these conditions there was an abrogation or inhibition of consciousness and a discharge of energy. Dr. Adey's references to the psychology of epilepsy had been of great interest. He would like to have light thrown on the psychology of *petit mal*.

DR. C. FARRAN-RIDGE said that in his experience of autopsies at Kew Mental Hospital he had found epilepsy associated with malformations and maldevelopments of various kinds and it did not occur in the absence of lesions of the brain. Some of these lesions were unequal hemispheres, microgyria and macrogyria, hydrocephalus, softening of the brain or portion of it, old encephalitis and old traumatic lesions. In the brains of twenty-four epileptics there had been no macroscopic evidence of gross pathological change in only eight instances. Dr. Farran-Ridge referred also to the peculiar temperament of epileptics. The fits were not necessarily prominent features; twilight states and epileptic equivalents had not been mentioned by the previous speakers. Collier and Kraepelin had thought that genuine epilepsy was produced by some metabolic dyscrasia. Patients who died in *status epilepticus* usually had excessive fat in the liver, kidney and heart.

DR. CLARENCE G. GODFREY thanked Dr. Robertson for a magnificent exposition of a most difficult subject. He referred to nocturnal epilepsy in which the turns occurred mainly during sleep. He wondered whether a psychic factor was responsible for these seizures. Epilepsy was a condition that caused a tremendous amount of harm and distress, and Dr. Godfrey wondered why philanthropists who were ready to contribute money for cancer or tuberculosis did not appear to help epileptics.

DR. JOHN WILLIAMS added his quota of thanks to Dr. Graeme Robertson. He referred to research work at the Talbot Colony for Epileptics and said that after this work had been at a standstill for some time, activity had latterly been in evidence. The Talbot Colony had been the dumping ground for chronic epileptics, most of them being in a deteriorated mental state. Dr. Williams considered that it was doubtful whether all the speakers had been talking about the same condition. He was interested to attempt to define the connecting link between traumatic epilepsy and the idiopathic type. It was probable that there was an epileptic tendency which could be activated by entirely different sets of circumstances. It might be postulated that the epileptic tendency was associated with birth traumata and reactivated later.

DR. A. P. DERHAM, after expressing his appreciation of the paper, said that many epileptics seemed to get into a hopeless state. The parents wished and expected the attacks to be minimized, but the drugs that were used to bring this about had an effect in contributing to the torpid state. He recalled that "Luminal" had come into general use in Melbourne in 1932, and that it was found to be of great benefit in comparison with bromides. Dr. Derham expressed the opinion that the converse held for certain children, and he was in the habit of alternating courses of bromides and phenobarbital and thought that he obtained maximal results with a minimal amount of dopiness. Dr. Derham next pointed out the extreme importance in the treatment of convulsions, which were otherwise unexplained, of the institution of anti-epileptic measures. A series of unconnected fits might not be recognized for quite a long time as evidence of true epilepsy. Dr. Derham also referred to the extraordinary disparity that could exist between the brain lesion and the epileptic manifestation. He remembered the presence of a very large fronto-parietal blood cyst in a child who had very frequent epileptic attacks. This child was the most intelligent child in the institution. Another patient mentioned by Dr. Derham was getting as much as four and a half grains daily of phenobarbital and was having many fits. The fits had stopped when the phenobarbital was stopped.

DR. F. KINGSLEY NORRIS, from the chair, offered the thanks of the Branch to Dr. Graeme Robertson for his address, and to the other speakers who had contributed to the discussion. Before calling on Dr. Robertson to reply, Dr. Norris asked two questions. He wanted an expression of opinion concerning the special investigations to which medical practitioners were justified in submitting a patient who was the subject of generalized convulsions, and he wished to know whether pyknolepsy could be excluded from the diagnosis if motor phenomena occurred.

Dr. Graeme Robertson, in reply, thanked the contributors to a discussion which he considered more than compensated for the defects in his paper. The discussion showed that epilepsy was a problem of a myriad facets, and the only connecting link between the many causes was the symptom. It might be stated that with increasing knowledge the idiopathic group would diminish in size. The knowledge gained from electroencephalograms might be of value in answering some of the questions which had been asked. For example, the presence of waves of large amplitude spreading in uninterrupted fashion over the whole cerebral cortex supported the old clinical grouping of *petit mal* and major attacks as forms of epilepsy.

The electroencephalogram showed that the cortical cells pulsated in unison when the subject was at mental rest with closed eyes in a dark room or in the early stages of sleep. There was thus this similarity between the discharge occurring under these conditions and that of epilepsy. Thus, perhaps, the development of an epileptic discharge was favoured by mental quietude and sleep, and this supported the clinical observation that epilepsy rarely occurred in such a situation as endangered a patient's life. Dr. Robertson therefore always advised mental and physical occupation for epileptics whenever it was possible. He believed that any slight risk was more than compensated for by the psychological gain when a group of patients was considered. He was interested in Dr. Adey's remarks on the psychology of epileptics. Dr. Robertson had noticed the intense sense of inferiority in those epileptics who came under his observation, probably at a much earlier stage than those seen by Dr. Adey. The continual mental knocks which these patients received during life might result in the epileptic temperament so lucidly described by Dr. Adey. He had not dealt with the

metabolic dyscrasias mentioned by Dr. Grieve, but he considered that they might be of considerable importance in the ætiology of epilepsy and were examples of factors which, when fully elucidated, could be expected to remove some of the cases from the idiopathic group. Cases in which fits were intimately associated with menstruation interested him very much. He confessed to an almost complete scotoma in knowledge in regard to the influence of snake venom and septic foci, but in regard to the latter he believed that, if there was obvious sepsis endangering health, steps should be taken to eradicate it.

He believed that the presence of twitching and convulsions excluded the diagnosis of pyknolepsy. Dr. Norris's other question was not easily answered without having the individual case under discussion. The author of a review of the subject had advocated opaque meals, should there be constipation or indigestion, estimation of basal metabolic rate, examination of cerebro-spinal fluid, radiography of the skull, and search for septic foci in the investigation of cases of epilepsy. Little would be learned from some of these investigations. X ray examination of the skull and examination of the cerebro-spinal fluid were usually carried out in patients admitted to the hospital for investigation, and in chosen cases, as in some indicated in the paper, encephalography was of very great value. In children he felt that the latter was rather of academic value; for the early diagnosis of a neoplasm of which there were no other signs or symptoms was much less likely to be made than in an adult. Idiopathic epilepsy was far commoner, and that resulting from cortical defects due to birth injury could usually be diagnosed from the associated physical signs.

Public Health.

A NOTICE has been published in the *New South Wales Government Gazette*, Number 118, of August 13, 1937, that undulant fever has been proclaimed an infectious disease within the meaning of, and for the purposes of, the *Public Health Act*, 1902, of New South Wales.

Post-Graduate Work.

PROTECTION OF THE CIVIL POPULATION AGAINST GAS ATTACK.

THE New South Wales Post-Graduate Committee in Medicine announces that it has arranged for a course of four lectures, dealing with the protection of the civil population against gas attack, to be given as set out hereunder:

Tuesday, September 21, 1937.—"Chemical Warfare and the General Requirements of a Civilian Gas Defence Scheme", Major J. J. N. McCall.

Thursday, September 23, 1937.—"Physiological Effects of War Gases and First-Aid Treatment for Gas Casualties", Professor H. W. Davies. "The Late Effects of Gas", Dr. C. K. Parkinson.

Tuesday, September 28, 1937.—"Blister Gases: Individual and Collective Protection; Material Decontamination", Major J. J. N. McCall.

Thursday, September 30, 1937.—"Organization, Scope and Control of Air Raid Precautions First-Aid Services", Major J. J. N. McCall.

The lectures will be delievered at the Robert H. Todd Assembly Hall, British Medical Association House, 135, Macquarie Street, Sydney, and will commence at 5 p.m. on each date mentioned.

No charge will be made for the lectures, which are open to members of the active and reserve forces, and to private medical practitioners.

COURSE OF INSTRUCTION IN DISEASES OF THE EAR, NOSE AND THROAT.

THE New South Wales Post-Graduate Committee in Medicine announces that, in conjunction with the Section of Oto-Rhino-Laryngology of the New South Wales Branch of the British Medical Association, it will hold a course of instruction in diseases of the ear, nose and throat, during a period of one week, commencing on Monday, October 11, 1937. The programme is as follows:

Monday, October 11.

(*The Royal North Shore Hospital of Sydney.*)

11 a.m. to 12 noon: "Anatomy and Physiology of Nose and Throat" (to include the larynx), Dr. A. L. Clowes.

12 noon to 1 p.m.: "Diseases of the Larynx and Tuberculous Disease of Ear, Nose and Throat", Dr. E. P. Blashki.

Tuesday, October 12.

(*The Royal Alexandra Hospital for Children.*)

11 a.m. to 12 noon: "Exanthemata and the Ear, Nose and Throat", Dr. Huff Johnston.

12 noon to 1 p.m.: "Sinusitis and Chronic Chest Infections", Dr. Ramsay Beavis.

(*The Robert H. Todd Assembly Hall, 135, Macquarie Street.*)

8 p.m.: "Œsophageal Obstruction", Dr. G. R. Halloran. "Foreign Bodies in the Air and Food Passages", Dr. E. P. Blashki.

Wednesday, October 13.

(*Saint Vincent's Hospital.*)

11 a.m. to 1 p.m.: "Diseases of Nose and Throat, including Neoplasms, with Indications for and Outlines of Treatment" (two lectures), Dr. H. Seaward Marsh and Dr. J. J. Woodburn.

Thursday, October 14.

(*The Royal Prince Alfred Hospital.*)

11 a.m. to 12 noon: "Introductory Otology", Dr. E. McA. Steel.

12 noon to 1 p.m.: "Advanced Otology", Dr. Ashleigh Davy.

Friday, October 15.

(*Sydney Hospital.*)

11 a.m. to 12 noon: "Testing of Function, including Auditory and Vestibular Functions", Dr. R. Francis.

12 noon to 1 p.m.: "Complications of Otological Lesions", Dr. H. S. Kirkland.

The fee for the course will be four guineas. The course will not be held unless six applications are received. The number of those attending will be limited to twelve. Those wishing to attend should apply to the Secretary, New South Wales Post-Graduate Committee in Medicine, the University of Sydney.

COURSE IN CLINICAL LABORATORY METHODS.

THE New South Wales Post-Graduate Committee in Medicine announces that a course in clinical laboratory methods, suitable for general practitioners, will be held during the five days Monday, October 25, to Friday, October 29, 1937, from 10 a.m. to 1 p.m. and from 2 p.m. to 4 p.m. For the most part it will take the form of tests and determinations which general practitioners themselves could do if necessary. In addition, if time allows, demonstrations of more difficult tests and estimations will be given.

The actual work done by those attending the course will to some extent be determined by the material that offers, but will probably include the following:

I. Hæmatology.

(*a*) Blood counts: methods of collection, staining and counting, including counting of platelets and reticulocytes and estimation of hæmoglobin content.
(*b*) Estimation of coagulation time and bleeding time.
(*c*) Estimation of sedimentation rate.
(*d*) Blood grouping.

II. Bacteriology.

(*a*) Collection of specimens for bacteriological examination.
(*b*) Routine methods of staining and identification of organisms from direct smears, cultures *et cetera*.
(*c*) Examination of hair *et cetera* for fungus.
(*d*) Examination for *Trichomonas vaginalis*.

III. Serology.

Collection of specimens for complement fixation tests.

IV. Biochemistry.

(i) Qualitative tests:
(*a*) Examination of urine for protein, reducing sugar, acetone bodies, bile, blood *et cetera*.
(*b*) Examination of the gastric contents for presence of lactic acid, hydrochloric acid, starch, bile, blood, food residues.
(*c*) Examination of fæces for occult blood.
(*d*) Examination of blood for bilirubin (Van den Bergh test).
(*e*) Examination of cerebro-spinal fluid for globulin.

(ii) Quantitative tests:
(*a*) Blood: determination of glucose, urea and creatinine content; determination of fragility.
(*b*) Gastric contents: titration of total and free acidity of fractional test meals.
(*c*) Urine: urea concentration and clearance tests for renal efficiency; reducing sugar.
(*d*) Cerebro-spinal fluid: determination of glucose and chlorides.

Demonstrations.

(i) Bacteriology:
(*a*) Preparation of vaccines.
(*b*) Methods of bacteriological examination of extracted teeth, enucleated tonsils *et cetera*.

(ii) Serology:
(*a*) Complement fixation tests (Wassermann test *et cetera*).
(*b*) Flocculation tests (Kahn test).

(iii) Biochemistry:
(*a*) Qualitative tests: Lange's colloidal gold reaction.
(*b*) Quantitative tests: estimation of the diastatic index; estimation of the blood calcium, phosphorus and cholesterol content; estimation of the basal metabolic rate.

(iv) Miscellaneous:
Aschheim-Zondek test (Friedman modification).
Schick test.
Casoni test.
Examination of the cerebro-spinal fluid (cytology *et cetera*).
Von Pirquet reaction.

The course will be held at the Kanematsu Institute, Sydney Hospital. Not more than eight members will be accepted for the course. Registration will be made in order of receipt of applications. The fee for the course is five guineas, and registration cannot be effected until the fee is paid. Registrations will be closed as soon as eight applications have been registered, and any applications that may thereafter be received will be given preference, in order of their receipt, for the filling of any vacancies that may occur.

Those wishing to attend should apply to the Secretary, New South Wales Post-Graduate Committee in Medicine, the University of Sydney.

COURSE IN CARDIOLOGY.

THE New South Wales Post-Graduate Committee in Medicine announces that it has arranged a course in cardiology, to be held during the five days commencing Monday, November 1, 1937.

The programme is as follows:

Monday, November 1.

(*The Royal Prince Alfred Hospital.*)

9.30 a.m. to 11 a.m.—"Anatomy and Physiology as Introduction to Clinical and Radiological Examination", Dr. J. Kempson Maddox.

11.15 a.m. to 12.30 p.m.—"Clinical Examination of Heart and Great Vessels and Significance of Symptoms", Dr. A. S. Walker.

2 p.m. to 5 p.m.—"Angina Pectoris: Diagnosis and Treatment" (clinical demonstration), Dr. M. C. Lidwell and Dr. L. Hughes.

Tuesday, November 2.

(*Sydney Hospital.*)

9.30 a.m. to 10.30 a.m.—"The Relation of Organic and Functional Cardiac Diseases", Dr. G. C. Willcocks.

10.45 a.m. to 12.30 p.m.—"*Résumé* of Clinical Electrocardiography, with Demonstration of Tracings", Dr. A. J. Hood Stobo.

2 p.m. to 5 p.m.—"Rheumatic Heart Disease and Sequelæ", "Chronic Endocarditis and Bacterial Endocarditis" (clinical demonstrations), Dr. Wilfred Evans and Dr. E. H. Stokes.

Wednesday, November 3.

(*The Royal Prince Alfred Hospital.*)

9.30 a.m. to 11 a.m.—"Cardio-Vascular Syphilis", Dr. J. Halliday.

11.15 a.m. to 12.30 p.m.—"Demonstration of Electrocardiograms", Dr. J. Kempson Maddox.

2 p.m. to 5 p.m.—"X Ray Examination of Heart and Great Vessels", Dr. H. R. Sear and officers of the radiological department.

Thursday, November 4.

(*Sydney Hospital.*)

9.30 a.m. to 11 a.m.—"Assessment of Cardiac Capacity in Industry, Pregnancy, Tuberculosis and Anæsthesia: Cardiac Efficiency Tests", Dr. Wilfred Evans.

11.15 a.m. to 12.30 p.m.—"Congenital Heart Disease", Dr. A. J. Hood Stobo.

2 p.m. to 5 p.m.—"Arterial Diseases and Hypertension" (clinical demonstrations), Dr. L. W. Dunlop and Dr. G. C. Willcocks.

Friday, November 5.

(*The Royal Prince Alfred Hospital.*)

9.30 a.m. to 11 a.m.—"Fluoroscopy of Heart and Great Vessels", staff of radiological department.

11.15 a.m. to 12.30 p.m.—Pathological demonstration, Dr. A. J. Canny.

2 p.m. to 5 p.m.—"Treatment of Cardiac Failure" (demonstration of cases illustrating various types), Dr. C. G. McDonald.

The fee for the complete course will be four guineas. The fee for the mornings only or for the afternoons only will be two guineas.

Applications for registration should be made to the Secretary, New South Wales Post-Graduate Committee in Medicine, the University of Sydney.

Correspondence.

MALARIA AND ITS TREATMENT BY THE GENERAL PRACTITIONER.

SIR: After reading Dr. A. E. Finckh's article on the treatment of malaria (THE MEDICAL JOURNAL OF AUSTRALIA of June 19, 1937) and Dr. W. L. Calov's letter on the subject (THE MEDICAL JOURNAL OF AUSTRALIA of July 3, 1937), I feel I must join Dr. Calov in support of quinine.

For six years I have held the position of medical officer in the field for the Bulolo Gold Dredging Company. During that time approximately 500 whites and 3,000 natives have passed through my hands for periods ranging from several months to several years, and I have treated practically every attack of malaria occurring among these.

Our natives are all recruited from hyper-endemic malarious areas and have a high tolerance for malaria, hence treatment is simple—they respond readily to quinine in small doses. I have treated five cases of cerebral malaria in native infants with intramuscular quinine with success.

Among whites I treat an average of 150 attacks of malarial fever each year; the ratio of tertian to subtertian is about 6 to 4. I have come across only one man and three women whom I could not handle with quinine alone. The man develops disturbances of vision on more than 15 grains of quinine daily. He does not respond to "Atebrin" alone, and he is controlled with a combination of the two. One of the women commences to menstruate after ten grains of quinine; she has had three attacks of fever in two years and has responded quite satisfactorily to "Atebrin"; by the fourth day the attacks subside, and after a five-day course there have been no relapses. She is my only case which completely vindicates the claims made for "Atebrin", although there may be others among those where I have not had occasion to go beyond quinine. The other two women are deaf, and a dosage of over 15 grains of quinine causes much discomfort. I have tried each twice with "Atebrin" alone. It fails to control an attack after five days; but when 15 grains of quinine are added daily, control is established.

Apart from these four patients, I now rely entirely on quinine alone for treatment of attacks and for prophylaxis against attacks. Occasionally after a severe attack I give a follow-up course of "Atebrin", in the hope that it will reinforce the quinine in preventing relapses, and where the spleen is more than usually enlarged I find that it reduces in size more rapidly with "Atebrin" than with quinine.

Aside from blackwater fever and the experimental use of the synthetic remedies, I had one other case where "Atebrin" alone had interesting results. I had a man in hospital suffering from headaches following frontal sinusitis. His temperature began to rise each second morning to between 37·2° and 37·8° C. (99° and 100° F.). After three such rises I gave him a course of "Atebrin". During the course his temperature continued to rise each second morning; on the day following the completion of the course he had a prolonged rigor, his temperature rose to 40·3° C. (104·6° F.), and he had bilious vomiting. Quinine was started, and beyond a rise of temperature to 38·0° C. (100·4° F.) on the next day but one, he had no further symptoms.

I have found "Plasmoquin" and "Atebrin" of no special value and quinine of great value in the after-treatment of blackwater fever. Of six cases, the first two received nothing until they developed attacks of malarial fever on the tenth and twelfth days, respectively, after the urine cleared. Each was given "Plasmoquin Compound", and neither responded until the quinine was increased to 15 grains per day. The other four were all given a five-day course of "Atebrin" early in the disease. One developed a malarial attack on the tenth day after his urine cleared, and had to be rapidly desensitized to quinine before it could be controlled. The next was type IV, and died on the thirteenth day after ten days' anuria. The last two were desensitized to quinine, commencing on the seventh day after the urine cleared, and neither developed any malaria.

During pregnancy all my patients have maintained their daily prophylactic quinine throughout, and all attacks have been treated with 30 grains daily without any ill-effects whatever. Two women who did not take prophylactic quinine aborted at ten weeks and fourteen weeks respectively, during the course of attacks of fever. During lactation I have twice found it necessary to wean the infants because quinine made the milk so distasteful that they refused to take it, and "Atebrin" could not satisfactorily control the mothers' malaria.

The worst case I have treated was a woman who never took prophylactic quinine and had been sick for a week before seeking treatment. She was vomiting almost continuously, with temperature fluctuating wildly between 37·8° and 40·0° C. (100° and 104° F.). She had 219,000 subtertian parasites per cubic millimetre. I gave her three injections of quinine intramuscularly, nine grains every twelve hours, and on the following morning her temperature was down to 37·2° C. (99° F.) and she commenced to eat and to take quinine by mouth. This is the only case where I have had to exceed two injections of quinine. An attack of cerebral malaria in a man was controlled by two injections followed by oral treatment.

As each new synthetic remedy came out, I tried a series of test cases. I found that "Plasmoquin Compound" was useless; "Quinoplasmoquin", which contains four and a half grains of quinine per dose, is slow and possessed of undesirable side effects and idiosyncrasies; "Plasmoquin Simplex" *plus* "Atebrin" is dangerous and not particularly effective; "Atebrin" alone is not particularly effective and possesses a high rate of idiosyncrasy; and now we have "Atebrin Musonate" for injection, which I am determined not to try under any circumstances.

Much as I dislike the flood of advertising matter which swamps my mail, I must admit that I welcome the entry of the Dutch Bureau for Propagating the Use of Quinine into the field of commercial propaganda.

Yours, etc.,

CARL GUNTHER.

Bulolo,
Territory of New Guinea,
August 5, 1937.

EPITHELIOMA OF THE LIP.

SIR: Quite a number of interesting papers *et cetera* have come to hand on the subject of epithelioma of the lip, with the almost simultaneous arrival of the current issue of THE MEDICAL JOURNAL OF AUSTRALIA, *The Australian and New Zealand Journal of Surgery* and the report of the eighth Australian Cancer Conference.

As it was not possible for me to attend this conference, I request the privilege of space in the journal to reply to certain matters raised by Dr. Molesworth and Dr. de Monchaux in their interesting articles.

Dr. Molesworth writes: "So far as this doctrine [the watch-and-wait] doing harm, as Dr. Meyers seems to imagine, I am sure it will provide a much larger proportion of ultimately successful results than a system which advocates the dissection of the gland-bearing areas of the neck in all cases of carcinoma of the lip."

Dr. de Monchaux writes: "Apropos of this [watch-and-wait policy] in a recent paper in which he strongly deprecates the wait-and-see attitude, Meyers of Brisbane records seven cases of lip carcinoma in support of this advocacy of routine block dissection."

Now I must disclaim any suggestion of such pontifical attitude. If Dr. Molesworth and Dr. de Monchaux really think that their statements are a reasonable commentary, I am much surprised, as they are more suggestive of the advocate than the scientist.

The question at issue was that of the treatment of the glandular areas in cases of epithelioma of the lip. I was not dealing with the question of treatment of the primary

growth, but of treatment of the glandular areas. My thesis was: "Subsequent treatment of the glandular areas should be by surgery or radiation."

May I draw the attention of my two colleagues to a statement in a paper written in conjunction with Dr. J. V. Duhig, and published in 1933 (*Cancer Research Journal of the University of Sydney*):

> In the past we have performed extensive block dissections of the neck (in cases of epithelioma of the lip) but latterly only the submental and submaxillary triangles have been removed, this operation being followed up by distance treatment to the side of the neck. Time will show whether this practice is as satisfactory as the complete block dissection.

I have to thank Dr. Molesworth for the information that he was told by Dr. Le Roux Berger that it was found on a survey of a large number of patients in whom the tumours were of all sizes and at all stages of development that only 20% of those who did not show involvement of the glands at the time of treatment of the primary growth subsequently provided recurrences in these glands. This was in 1927, and applied to Frenchmen, I presume. What is the position in regard to Australians or to Dr. de Monchaux's friends, the Greenlanders, I cannot say.

In the event of Dr. Molesworth's being questioned by a patient about the possibility of recurrence of epithelioma of the lip, the doctor would answer (according to the authority he quoted) that on the average the possibility of recurrence was not less than one in five, and that any particular patient might be the unlucky one.

An alternative reply from Dr. Molesworth might be that he selects his patients for treatment, and this may be just what Dr. Molesworth does—and, one may say, rightly so, but (if he does select his patients in regard to treatment of epithelioma of the lip) one would suggest that he make this fact plain when he writes upon the subject.

In regard to Dr. de Monchaux's carefully prepared statistics, I am afraid that there are so few of them dealing with patients treated long enough for a five years' period to have elapsed since the commencement, that we can only look upon them in the nature of a progress report.

Dr. de Monchaux states, in regard to grading: "like Broders, we found the extreme types (1 and 4) least common in our series". Ward and Smith ("Recent Advances in Radium", 1933, page 172) state according to Broders 75% fall into Grades 1 and 2.

I agree with Dr. de Monchaux as to the necessity for careful recording, and think it only fair that, in any comparisons of treatment, we should make every effort to make the comparison a fair one.

Looking at the matter generally, we should be more interested in our failures than our successes. We must attempt to attain 100% of good results in early cases. It must be remembered that we get local recurrences after the treatment of the primary lesion by radium and by surgery even in the best clinics. What is the reason that we do not always get a beautiful supple result of healing? If we could prevent the keloid we might prevent recurrence. A further query: Are the good results (even if the cases are selected) of Dr. Molesworth due in part to a general biological action of the X rays? Again, what is the nature of the change in the small submental glands which apparently commences as a hyperplasia? Is this change seen in vertebrates other than man?

May I say in conclusion, while thanking Dr. Molesworth and Dr. de Monchaux for their papers, that I either personally or with the help of my colleagues make use of the treatment that seems best for the individual case, be it by means of radium, surgery, X rays, Chaoul method, diathermy *et cetera*; but I feel that I shall be voicing the opinion of reasonable people in advocating treatment of the glandular areas in all cases of epithelioma of the lip.

Yours, etc.,

E. S. MEYERS.

Wickham Terrace,
Brisbane,
August 8, 1937.

WHY SYPHILIS AND TUBERCULOSIS ARE VERY CHRONIC INFECTIONS.

SIR: The organisms causing these diseases, entering the body, proliferate and cause disease provided they are of a strain suitable for development. If not, they die out and are thrown off.

If they proliferate, the tissues react and lesions are produced. But a large number of the germs are excreted per medium of the lymphatics, opening on the external or internal surfaces of the body. If the rate of excretion is greater by the skin, which is the case in hot climates, the infection is benign and in many cases the patient appears to be cured.

In cold climates excretion by the respiratory, alimentary and urinary tracts prevails; but in many cases it is not sufficient to make up for the loss of skin action. But the trouble is that, whereas the germs thrown off externally are definitely lost to the body, those in the above-mentioned tracts can be excreted again and again—a vicious circle is established.

Arsenic and bismuth have no direct action on either visible or infravisible forms of the parasite of syphilis. They act on the reticulo-endothelial system, preventing stasis and stimulating the movement of the organisms in the lymphatic system. Their action might be compared with that of the traffic policeman.

I suggest the foregoing as a partial explanation of the reason why these infections are so chronic and so difficult to cure.

Yours, etc.,

J. MORRIS ROE.

Brisbane,
August 10, 1937.

REPLACING GUESSWORK AND INSTINCT BY CALCULATION IN MOTOR DRIVING.

SIR: Today hospital authorities complain that accommodation is denied the urgently sick by the occupation of beds by victims of motor accidents. It does not seem to be sufficiently realized that the public require education in mechanical as well as traffic laws. Though scientific advice and safeguards are tendered the custodian of the circular saw and other potentially lethal industrial devices, complete familiarity with the traffic laws leaves much to be desired in the complete education of the motorist ignorant of certain simple laws of mechanics.

A few suggestions made by the writer were considered of sufficient moment by the Royal Automobile Club of Victoria to be promulgated in their official journal and in newspapers throughout Victoria. I will quote these suggestions and a brief account of fatal motor accidents which would have been obviated by their adoption.

1. On main roads, even where there are no crossings, accidents are constantly occurring. Many accidents under such conditions are due to overtaking another car going the same way, and in the face of a car coming from the opposite direction. How many drivers realize that in meeting an oncoming car they are doing so at the combined speeds of their own car and the other one? For instance, if both are travelling at 40 miles an hour, they are approaching each other at the speed of 80 miles an hour. Accidents here are due to failure to evade the oncoming car, or swerving in and out at a speed too great for the wheels to hold the road.

Overtaking can be justified only when the road is in good order and is clear for a long way ahead of oncoming cars, because it is next to impossible to judge the speed at which they are approaching.

2. In regard to skidding, if a motorist has learnt the simple laws of mechanics, he knows in advance what is only learnt otherwise by instinct after years of experience. When a car weighing one ton is travelling at 40 miles an hour, it travels forward with a force of 60 foot tons, or simply tons of pressure, in the language of the laity. If a car is suddenly switched in a sideways direction, this

60 tons of pressure still travels forward; but it now acts across the car, hence the skid or turning turtle two or three times. If the tires burst, or the wheels are on loose gravel at the side of the road, control is lost and the car finishes upside-down against a fence, in a ditch or on the wrong side of the road in the face of oncoming traffic. Who could feel safe driving what is a 50-ton hammer on wheels if he knew these facts or had old tires?

3. If a car is travelling against the regulations at 40 miles per hour, it covers 100 yards in five seconds. When you enter a main road from a side street, a car travelling at this speed is "on you before you see it". This sudden appearance of a fast car from "nowhere" is the cause of most collisions, and again of swerves into plantations, at intersections.

In the first accident reported last week-end, two people were killed and three seriously injured for the following reasons.

> The accident occurred when Mr. ——'s car was passing another car. A tire on Mr. ——'s car blew out, and the back of the car swung off the road into a tree. The car was wrecked.

In the second accident one was killed and three were injured.

> The car was swerved to avoid a cyclist near the railway bridge, about half a mile north of the Essendon aerodrome. The car swerved off the narrow strip of bitumen, and as Mr. —— turned it back onto the bitumen it skidded and overturned on the roadway. Resting on the crushed hood, the car pinned all the occupants.

In the third, one man was killed "negotiating what is known as an *S* turn, when the car left the road, struck a tree, and overturned. Mr. —— was killed outright."

These facts speak for themselves and surely demand incorporation of the simple mechanical facts surveyed in the official education of motorists, and in guides issued for this purpose.

Yours, etc.,

Melbourne, "PRO-BONO."
Undated.

THE TALBOT COLONY FOR EPILEPTICS.

SIR: In view of a report furnished by the medical officers of the above colony to this council, it has been decided that it is desirable and necessary, in the best interests of the patients of the colony, to enforce the conditions of admission, particularly those relating to ineligibles, as set out in the original scheme of the colony.

We feel it would help the colony if you could see your way to publish these conditions in your journal, so that they would be brought under the notice of all members of the profession.

The object of the Talbot Colony is to establish cottages on the colony system, where persons suffering from epilepsy, yet capable of employment, may enjoy the advantage of regular life with healthy surroundings, and where, under the necessary supervision, they may be educated, industrially trained or suitably employed, with a view to cure and ultimate return to active life. The Talbot Colony is thus an industrial institution and is not a hospital for epileptics or a retreat for incurable invalids. The colony possesses unique facilities in this direction and is anxious to consider the admission of suitable patients.

The ineligible cases are as follows:

(*a*) Those who through mental or moral deficiency would be incapable of participating in and benefiting by the mode of life at the colony.

(*b*) Those who are liable to outbreaks of insanity or to dangerous impulses.

(*c*) Those who from habitual awkwardness of disposition or excessive irritability of temper would be a source of annoyance to their fellow "colonists".

(*d*) Those who through physical disablement or extreme infirmity are unable to engage in any kind of occupation or are incapable of dressing themselves or attending to their own personal wants. Mere physical infirmity does not disqualify.

(*e*) Those who suffer from any other disease of such a nature as to render them unsuitable to be inmates of the homes.

Any further information you may require I would be pleased to supply.

Yours, etc.,

F. BROWNFIELD,
Secretary.

The Talbot Colony for Epileptics,
53, Russell Street,
Melbourne, C.1,
July 27, 1937.

Obituary.

WILLIAM WITHERS EWBANK.

WE regret to announce the death of Dr. William Withers Ewbank, which occurred on August 11, 1937, at Caulfield, Victoria.

JULIAN GILBERT DESAILLY.

WE regret to announce the death of Dr. Julian Gilbert Desailly, which occurred on August 15, 1937, at Middle Brighton, Victoria.

RAYMOND CHARLES LANE.

WE regret to announce the death of Dr. Raymond Charles Lane, which occurred on August 18, 1937, at Strathfield, New South Wales.

HARRY PAYNTER SLOGGETT.

WE regret to announce the death of Dr. Harry Paynter Sloggett, which occurred on August 18, 1937, at Middle Park, Victoria.

Books Received.

THE DESIGN OF EXPERIMENTS, by R. A. Fisher, Sc.D., F.R.S.; Second Edition; 1937. Edinburgh and London: Oliver and Boyd. Demy 8vo, pp. 272. Price; 12s. 6d. net.

HANDBOOK OF DIETS, by R. M. Simmonds, S.R.N., with a foreword by Lord Dawson of Penn, P.C., G.C.V.O., K.C.B., M.D.; Second Edition; 1937. London: William Heinemann (Medical Books) Limited. Demy 8vo, pp. 171. Price: 7s. 6d. net.

ANNUAL REPORT OF THE SURGEON-GENERAL OF THE PUBLIC HEALTH SERVICE OF THE UNITED STATES FOR THE FISCAL YEAR 1936; 1936. Washington: United States Government Printing Office. Medium 8vo, pp. 164. Price: $1.00.

AN INTRODUCTION TO COMPARATIVE BIOCHEMISTRY, by E. Baldwin, B.A., Ph.D., with a foreword by Professor Sir F. G. Hopkins, F.R.S.; 1937. Cambridge: The University Press. Crown 8vo, pp. 130. Price: 5s. net.

ROSE AND CARLESS MANUAL OF SURGERY FOR STUDENTS AND PRACTITIONERS, by C. P. G. Wakeley, D.Sc., F.R.C.S., F.R.S., and J. B. Hunter, M.C., M.Chir., F.R.C.S.; Fifteenth Edition, in two volumes; 1937. London: Baillière, Tindall and Cox. Royal 8vo, pp. 1630, with 948 figures and 18 colour plates. Price: 30s. net.

MEDICAL UROLOGY, by I. S. Koll, B.S., M.D., F.A.C.S.; 1937. St. Louis: The C. V. Mosby Company; Australia: W. Ramsay (Surgical) Proprietary Limited. Medium 8vo, pp. 421, with 92 text illustrations and 6 colour plates. Price: 30s. net.

PROGNOSIS; Volume II: 1937. London: The Lancet Limited. Demy 8vo, pp. 430. Price: 10s. 6d. net.
CATECHISM SERIES. ELEMENTARY GENETICS FOR STUDENTS OF BIOLOGY AND MEDICINE, by H. Grüneberg, Ph.D., M.D.; 1937. Edinburgh: E. and S. Livingstone. Crown 8vo, pp. 87. Price: 1s. 6d. net.

Diary for the Month.

SEPT. 1.—Western Australian Branch, B.M.A.: Council.
SEPT. 1.—Victorian Branch, B.M.A.: Branch.
SEPT. 2.—South Australian Branch, B.M.A.: Council.
SEPT. 3.—Queensland Branch, B.M.A.: Branch (Jackson Lecture).
SEPT. 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.
SEPT. 10.—Queensland Branch, B.M.A.: Council.
SEPT. 14.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
SEPT. 15.—Western Australian Branch, B.M.A.: Branch.
SEPT. 21.—New South Wales Branch, B.M.A.: Ethics Committee.
SEPT. 22.—Victorian Branch, B.M.A.: Council.
SEPT. 23.—New South Wales Branch, B.M.A.: Clinical Meeting.
SEPT. 24.—Queensland Branch, B.M.A.: Council.
SEPT. 28.—New South Wales Branch, B.M.A.: Medical Politics Committee.
SEPT. 30.—South Australian Branch, B.M.A.: Branch.
SEPT. 30.—New South Wales Branch, B.M.A.: Branch.

Medical Appointments.

Dr. G. T. Hunter has been appointed Government Medical Officer at Moree, New South Wales.

* * *

Dr. H. W. Wunderly has been appointed Honorary Physician at the Adelaide Hospital, Adelaide, South Australia.

* * *

The following appointments have been made in the office of the Director-General of Public Health of New South Wales: Dr. F. H. H. Wilson, Deputy Medical Superintendent; Dr. N. J. Symington, Senior Medical Officer; Dr. R. R. Bye, Junior Medical Officer; Dr. E. B. Jones, Medical Officer.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," pages xvi to xix.

AYR HOSPITALS BOARD, AYR, QUEENSLAND: Junior Medical Officer.

BRISBANE AND SOUTH COAST HOSPITALS BOARD, QUEENSLAND: Honorary Officers.

PUBLIC SERVICE BOARD, ADELAIDE, SOUTH AUSTRALIA: Medical Inspector of Schools.

PUBLIC SERVICE OF THE NORTHERN TERRITORY: Medical Officer.

ROYAL MELBOURNE HOSPITAL, MELBOURNE, VICTORIA: Honorary Officers.

ROYAL NORTH SHORE HOSPITAL OF SYDNEY, NEW SOUTH WALES: Honorary Clinical Assistant.

SAINT MARGARET'S HOSPITAL FOR WOMEN, SYDNEY, NEW SOUTH WALES: House Surgeon, Honorary Officers.

SYDNEY HOSPITAL, SYDNEY, NEW SOUTH WALES: Honorary Clinical Assistants.

THE MUNICIPAL COUNCIL OF SYDNEY, NEW SOUTH WALES: Junior Medical Officer.

THE UNIVERSITY OF MELBOURNE, VICTORIA: Professor of Anatomy.

THE WOMEN'S HOSPITAL, CROWN STREET, SYDNEY, NEW SOUTH WALES: Resident Medical Officer.

VICTORIAN EYE AND EAR HOSPITAL, MELBOURNE, VICTORIA: Resident Surgeon.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCHES.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 135 Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company Limited. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17	Brisbane Associate Friendly Societies' Medical Institute. Proserpine District Hospital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 178 North Terrace, Adelaide.	All Lodge appointments in South Australia. All contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 205, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.

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